

# AGARD

ADVISORY GROUP FOR AEROSPACE RESEARCH & DEVELOPMENT

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**AGARD LECTURE SERIES 189**

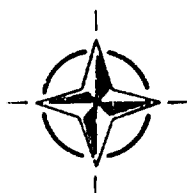
## Cardiopulmonary Aspects in Aerospace Medicine

(Les Aspects Cardiopulmonaires en  
Médecine Aérospatiale)

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North Atlantic Treaty Organization  
Organisation du Traité de l'Atlantique Nord

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# The Mission of AGARD

According to its Charter, the mission of AGARD is to bring together the leading personalities of the NATO nations in the fields of science and technology relating to aerospace for the following purposes:

- Recommending effective ways for the member nations to use their research and development capabilities for the common benefit of the NATO community;
- Providing scientific and technical advice and assistance to the Military Committee in the field of aerospace research and development (with particular regard to its military application);
- Continuously stimulating advances in the aerospace sciences relevant to strengthening the common defence posture;
- Improving the co-operation among member nations in aerospace research and development;
- Exchange of scientific and technical information;
- Providing assistance to member nations for the purpose of increasing their scientific and technical potential;
- Rendering scientific and technical assistance, as requested, to other NATO bodies and to member nations in connection with research and development problems in the aerospace field.

The highest authority within AGARD is the National Delegates Board consisting of officially appointed senior representatives from each member nation. The mission of AGARD is carried out through the Panels which are composed of experts appointed by the National Delegates, the Consultant and Exchange Programme and the Aerospace Applications Studies Programme. The results of AGARD work are reported to the member nations and the NATO Authorities through the AGARD series of publications of which this is one.

Participation in AGARD activities is by invitation only and is normally limited to citizens of the NATO nations.

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# Abstract

This Lecture Series will update the information presented in the 1987 AGARD Short Course on the Cardiopulmonary Aspects of Aerospace Medicine, and will be of primary relevance to military internists and cardiologists with an interest in aviation medicine, and to military Flight Surgeons. Topics to be discussed will include techniques for and utility of screening for asymptomatic coronary artery disease in an aircrew population; the aeromedical disposition of aviators with coronary disease; the usefulness of primary coronary prevention programmes, based on data from recent intervention studies and meta-analyses; the aeromedical implications of ECG abnormalities and structural/valvular cardiac anomalies based on data from USAF/AL Study Groups; the utility of screening aircrew candidates with echocardiography and echocardiographic findings in trained aircrew; hypertension in aircrew; and the aeromedical implications of a number of pulmonary diseases, notably asthma and airway hyper-reactivity, obstructive pulmonary disease, pneumothorax and sarcoid. The Lecture Series will be designed to be interactive rather than strictly didactic to encourage discussion of problems particular to participating NATO countries.

This Lecture Series, sponsored by the Aerospace Medical Panel, has been implemented by the Consultant and Exchange Programme.

# Abrégé

Ce cycle de conférences représente une mise à jour des informations présentées lors du Cours AGARD sur les aspects cardiopulmonaires de la médecine aérospatiale organisé en 1987. Il est destiné principalement aux internes et aux cardiologues militaires qui s'intéressent à la médecine aéronautique, ainsi qu'aux médecins du personnel navigant.

Les sujets qui seront examinés comprennent les techniques et l'utilité du dépistage des maladies asymptomatiques des artères coronaires chez les pilotes; la disposition aéromédicale des aviateurs atteints de maladies coronaires; l'intérêt des campagnes de prévention primaire des maladies coronaires, sur la base des données obtenues suite aux expérimentations et méta-analyses effectuées récemment; les conséquences aéromédicales d'anomalies ECG et d'anomalies cardiaques structurales/valvulaires, sur la base des résultats des travaux des groupes d'études USAF/AL; l'utilité du dépistage des futurs équipages à l'aide de résultats échocardiographiques et d'échocardiographie relatifs à des équipages expérimentés; l'hypertension chez les pilotes; ainsi que les conséquences aéromédicales d'un certain nombre de maladies pulmonaires et notamment l'asthme, la hyper-réactivité des voies respiratoires, les maladies respiratoires obstructives, le pneumothorax et la sarcoidose.

Ce cycle de conférences revêtira un caractère interactif plutôt que didactique, afin de favoriser la discussion de problèmes spécifiques aux pays de l'OTAN participant à la conférence.

Ce cycle de conférences est organisé dans le cadre du programme des consultants et des échanges, sous l'égide du Panel de médecine aérospatiale.

## Preface

In 1987 the AGARD Aerospace Medical Panel (AMP) sponsored a Short Course on the Cardiopulmonary Aspects of Aerospace Medicine. The course lecture notes were published as AGARD-R-758 in 1987. They provided state-of-the-art information to NATO Flight Surgeons on aviation cardiology and respirology, and have been used extensively by many NATO countries since in teaching aviation medicine. The Lecture Series prompted lively debate in all four locations, and the discussions were taped and published as AGARD-R-758 (Addendum). Together with this publication, these reports provide a comprehensive information-base in aviation cardiology and pulmonology.

The 1987 Short Course was conceived and organized by Colonel J.R. Hickman Jr, then Chief of the Clinical Sciences Division at the USAF School of Aerospace Medicine. He believed that aeromedical decision-making should be based on a scientific approach and he considered it important that NATO Flight Surgeons be familiarized with the information and data required to make information-based decisions. Unfortunately, Dr Hickman is unable to participate in this Lecture Series but it is the hope of the Director and staff that we can maintain his high standards of teaching.

At the time of the first course, it was proposed that an update course be run every five or six years to keep NATO Flight Surgeons abreast of current developments in aviation cardiology and pulmonology. Since the 1987 Lecture Series, there have been a number of new developments in aviation cardiology. The purpose of this current Lecture Series is to disseminate this information and to provide a format for discussion of current cardiovascular and pulmonary aeromedical issues.

Commander Gary W. Gray, MD, FRCPC  
Lecture Series 189 Director

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## CARDIOVASCULAR AND PULMONARY DISEASE IN NATO AIRCREW AN OVERVIEW

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In 1987, the AGARD Aeromedical Panel (AMP) sponsored a Short Course on the Cardiopulmonary Aspects of Aerospace Medicine (1). The aim of the course was to disseminate current information about the aeromedical implications of cardiac and pulmonary conditions to NATO Flight Surgeons.

At the time of the first course, it was proposed that an update course be run every five to six years to keep NATO Flight Surgeons abreast of current developments in aviation cardiology and pulmonology. Since the 1987 Lecture Series, there have been a number of new developments in aviation cardiology. The purpose of this Lecture Series is to disseminate this information.

### CARDIOPULMONARY DISEASE IN NATO AIRCREW

Cardiovascular disease is the most common cause of morbidity and mortality in persons of aircrew age in developed nations and is the largest medical reason for removing aircrew from flying duties in most published series (2, 3). The incidence of pulmonary disease is smaller but the magnitude of these problems in NATO aircrew has not been documented.

In preparation for this Lecture Series, a questionnaire was sent to an AMP representative from each of the NATO countries. The questionnaire sought information concerning the incidence of cardiopulmonary disease in NATO aircrew in the calendar year 1991. Methods and frequency of screening for cardiac and pulmonary disease was also requested.

Information was received from 14 aeromedical agencies in 12 countries providing a denominator of 87665 aircrew. This total represents responses only from those agencies from which sufficient data was available. Although the questionnaire requested information on pilots only, some agencies included information on other aircrew who undergo regular periodic screening and this data has been included in the database.

The rapid acquisition of this large database denominator demonstrates the significant epidemiologic power available when data from NATO agencies is combined.

Table 1 shows the overall incidence of medical restrictions and groundings during the calendar year

1991 in the survey, and the rates for cardiovascular and pulmonary disease. Overall, 1.2% of the aircrew population surveyed were removed from flying duties or were operationally restricted for medical reasons in 1991. One third of these were because of cardiovascular disease, while only 4.8% were due to pulmonary disease.

NATO AIRCREW SURVEY			
TOTAL AIRCREW		87665	
	No.	Total	%
GROUND	573		0.65
RESTRICT	487		0.55
		1060	
CARDIOVASCULAR DISEASE			
GROUND	258		45
RESTRICT	96		19.7
		354	
PULMONARY DISEASE			
GROUND	18		3.1
RESTRICT	33		6.8
		51	
Table 1. Medical restrictions and groundings in a one year period in a sample population of 87665 NATO aircrew			

The overall grounding rate for medical reasons was 0.65% of those grounded. Cardiovascular disease accounted for almost half (45%) while only 3.1% of those grounded were due to pulmonary disease.

While it is reassuring to discover that the incidence of medical grounding is low, given the very high cost of training aircrew to operational readiness, there remains a significant challenge to research and identify the scientific rationale for grounding or restricting aircrew because of cardiac or pulmonary disorders.

### CARDIOVASCULAR DISEASE

In Table 2, the various reasons for flying restrictions and groundings due to cardiovascular disease are tabulated. Cardiac arrhythmias were by far the most common reason for a medical restriction/grounding, constituting almost half (46.7%) of those grounded for cardiovascular disease. Interestingly, more aircrew were grounded/restricted for hypertension than for

coronary heart disease. Twice as many were grounded/restricted for arrhythmias as for coronary heart disease. Valvular heart disease was a relatively uncommon cause for grounding/restriction, accounting for only 7% of the total. "Other" reasons were uncommon and included heart transplant, myocardial sarcoid, and hypertrophic cardiomyopathy.

CARDIOVASCULAR DISEASE			
	No.	TOTAL	%
		354	33.3
GROUND	258		45
RESTRICT	96		19.7
CORONARY HEART DISEASE			
		71	20
GROUND	48		18.6
RESTRICT	23		23.9
VALVULAR HEART DISEASE			
		25	7
GROUND	15		5.8
RESTRICT	10		10.4
ARRHYTHMIAS			
		142	40.1
GROUND	118		45.7
RESTRICT	24		25.0
HYPERTENSION			
		86	24.3
GROUND	46		17.8
RESTRICT	40		41.7
OTHER CARDIAC			
		25	7.1
GROUND	14		5.4
RESTRICT	11		11.5

Table 2. Incidence of groundings and restrictions for cardiovascular disease in a one year period in 87665 NATO aircrew

From this information, it is clear that our aeromedical efforts should be directed towards clarifying the aeromedical significance of various arrhythmias, and to identifying treatment approaches for hypertension which are compatible with continuing flying duties. There have been some significant recent changes in the recommended aeromedical disposition for arrhythmias, and new advances in the investigation and treatment of hypertension which should reduce the medical attrition of aircrew for these reasons. The papers by Dr. Celio and Dr. Hull later in this report provide new information on these topics.

## PULMONARY DISEASE

In contrast, pulmonary disease accounted for only 4.8% of the total medical reasons for grounding/restriction. Asthma was the most common cause by far. In the population of 85,667 aircrew, only one was grounded and another restricted because of chronic obstructive pulmonary disease (COPD). Pneumothorax, too, was surprisingly uncommon in this large population group. "Other" reasons included sarcoid, extrinsic allergic alveolitis, and a heart-lung transplant.

PULMONARY DISEASE			
	No.	TOTAL	%
		51	4.8
GROUND	18		3.1
RESTRICT	33		6.8
ASTHMA			
		24	47
GROUND	14		77.8
RESTRICT	10		30.3
COPD			
		2	3.9
GROUND	1		5.5
RESTRICT	10		30.3
PNEUMOTHORAX			
		2	3.9
GROUND	1		11.1
RESTRICT	0		
OTHER			
		23	45
GROUND	2		11.1
RESTRICT	21		67

TABLE 3. Groundings and restrictions for pulmonary disease in a year period in 87665 NATO aircrew

While asthma may present for the first time in adults, it rarely occurs without some footprints earlier in life. This information that asthma represents the most prevalent pulmonary problem resulting in grounding emphasizes the importance of detecting airway hyper-reactivity at the time of pilot selection. This problem is further discussed in the paper on "Asthma in Aircrew"

## SCREENING FOR CARDIOVASCULAR DISEASE IN NATO AIRCREW

In Table 4, the screening methods used for pilot selection in fourteen NATO aeromedical agencies are outlined. Interestingly, half include an exercise electrocardiogram as part of the initial screen; in two countries, aerobic



capacity is measured and forms part of the selection criteria.

SELECTION SCREENING		
	YES	NO
RESTING ECG	14	
EXERCISE ECG	7	7
LIPIDS	12	2
ECHOCARDIOGRAM	5	9
CHEST X-RAY	13	1
PULMONARY FUNCTION	11	3
OTHER		
EXERCISE CAPACITY	2	

Table 4.

Given that arrhythmias form the major cardiovascular cause of grounding of trained aircrew, the inclusion of a screening echocardiogram to screen for structural substrates for arrhythmias and exercise study for arrhythmias would seem to be cost-effective techniques. 24 ambulatory ECG monitoring is not used by any NATO country on initial screening.

Regarding mitral valve prolapse and bicuspid aortic valve on initial selection, ten of thirteen agencies responding to the question disqualify candidates with MVP on selection; two countries allow candidates with MVP to enter training, and a third into non-fighter aircraft only. Seven of ten agencies responding to the question of bicuspid aortic valve disqualify candidates if the condition is discovered on selection, but three allow candidates into training.

Most countries include lipid screening on initial selection, but the criteria for rejection vary considerably and are shown in Table 5. The values are given in mg/dl. Major Rodriguez (4) provided further information about cardiovascular risk factors in NATO aircrew in his keynote address to the 1992 Spring AMP meeting.

SELECTION LIPID SCREENING			
CHOL	TRIG	HDL	CHOL/HDL
200	200	>35	<6
300			
250			
250			
300			
220			
*230			<6.7
*200			<6
mean=250			
* other conditions apply if limits exceeded			

Table 5. Lipid selection criteria in 8 NATO countries

The average maximum limit for total cholesterol is 250 mg%, or 6.5 mmol/L, which at the usual age of pilot

selection represents an extreme value, well beyond the 95th percentile for age based on the North American Lipid Research Clinic prevalence data. All agencies allow candidates to re-apply after diet/life-style modification if the selection criteria are then met.

#### PERIODIC CARDIOVASCULAR and PULMONARY SCREENING

The periodicity for cardiovascular screening varies considerably amongst the 14 NATO aeromedical agencies who responded to this part of the questionnaire. The results are summarized in Table 6 (following references)

**PHYSICAL EXAMINATIONS** are done annually by most, but vary from every six months to biannually. One agency does clinical examinations only every three years to age 40 then annually after 40. Two agencies have a biannual system with an abbreviated medical on the off year.

**ELECTROCARDIOGRAMS** are done annually by most agencies. In two countries, they are done routinely every six months. Several agencies have a staggered system with increasing frequency with age e.g. every five years to age 40, then biannually to age 50, then annually.

**LIPIDS** are measured annually by most agencies. Two measure them every six months

**EXERCISE STRESS TESTS** are not done routinely by 8 of 14 agencies, but do form part of the routine examination in 6 countries. Periodicity varies from annually in two countries, annually after age 40 in one, and every six years to age 40 then every 3 years thereafter in one.

**PULMONARY FUNCTION TESTING** is done routinely in eight countries, but is not part of the routine examination in five.

**CHEST X-RAYS** continue to be part of the routine annual examination in four countries.

**ECHOCARDIOGRAMS** are not done as part of the routine periodic examination by any of the reporting agencies.

**G-TOLERANCE.** Only one country polled reported G-tolerance as a criteria for pilot selection, although G-training for experienced pilots is carried out by many agencies.

#### FLIGHT SAFETY IMPLICATIONS OF CARDIOPULMONARY DISEASE

Interestingly, only one agency reported a possible link between cardiopulmonary disease and an aircraft accident in the past decade. Two accidents were reported in which sudden incapacitation was

considered the most probable cause with cardiovascular disease suspected, but a direct link with cardiovascular disease was not possible because of lack of material for post-mortem. In one other accident attributed to pilot error the aircraft struck the ground and the autopsy showed an 80% lesion of the left anterior descending coronary artery.

#### PHYSIOLOGIC CONSIDERATIONS OF CARDIOPULMONARY DISEASE

Military air operations create physiologic stresses not encountered in most civilian operations, including high sustained G and the possibility of rapid cabin decompression due to enemy action. Current generation fighter aircraft can generate G-onset rates which produce completely unheralded G-induced loss of consciousness (G-LOC), and can sustain radial acceleration producing extreme levels of sustained +Gz. They can operate at altitudes in which protection against loss of cabin pressurization requires either a full pressure suit or extreme levels of positive mask pressure to maintain an adequate inspired oxygen tension.

Life support equipment development is progressing to keep pace with the engineering technology. With extended-bladder G-suits and positive pressure assisted-breathing, protection to +Gz now exceeds 12 Gz under experimental conditions.

Protection against sudden depressurization at high altitudes involves positive pressure breathing to pressures of 80 mmHg with pressure breathing jerkin and G-suit counterpressure.

The performance capabilities of the new generation aircraft and life-support equipment raise a host of questions about the man in the system. The envelope between what is an abnormal or pathologic physiologic reaction, and what is normal in such unusual environments is less well defined.

#### CARDIAC CONCERNS

Distortion of cardiac structure and function under high levels of sustained +Gz has been demonstrated by echocardiographic studies in the human centrifuge (5). Repeated exposure HSG may produce anomalies in cardiac structure; an early report suggested that right ventricular enlargement was more prevalent in fighter pilots than a group of control transport pilots (6). This possibility is presently being investigated by the AGARD Aeromedical Panel through Working Group 18 "Echocardiography in NATO Aircrew" which will be concluded and reported in 1994. Dr. Celio reports some early data from this project in his presentation on echocardiography later in this monograph.

Cardiac arrhythmias which clinically would be considered pathologic occur with surprising frequency in aircrew and experimental subjects on the centrifuge and presumably occur with similar frequency in the air (7,8,9). The arrhythmias likely reflect the rapid and marked changes in vagal and sympathetic activity resulting from G-onset and offset as well as the marked alterations in cardiac chamber geometry with the rapid changes in pre-load and afterload. At DCIEM, we have observed episodes of non-sustained ventricular tachycardia, paroxysmal supraventricular tachycardias and atrial fibrillation, as well as prolonged pauses and sinus arrest during G-offset (Figures 1 and 2) in the DCIEM centrifuge.

A recent observation of operational concern is a marked decrease in G-tolerance on transition from negative to positive Gz with G-LOC occurring at only +3 to +4 Gz in subjects transitioning from negative Gz (10,11). The exposure to -Gz causes a marked sinus bradycardia which Banks termed "bunt bradycardia" and which is presumably due to baroreceptor stimulation. The increased vagal activity leaves the individual particularly compromised and physiologically unprepared for transition to +Gz.

#### PULMONARY CONCERNS

The elastic and distensible lungs are undoubtedly the organs most susceptible to the effects of changes in G forces with radial acceleration. Even with the normal +1Gz, pulmonary architecture is distorted with distension of apical alveoli and compression of alveoli at lung bases. With exposure to higher levels of +Gz, lung architecture becomes increasingly distorted (12) and one would expect to see disruption of lung tissue. This danger has been clearly expressed by Dr. Earl Wood (1314), who reported a case of acute lung rupture in the human centrifuge.

Human subjects on the DCIEM centrifuge at very high levels of +Gz report an unusual respiratory sensation of dyspnea even with pressure-assisted breathing; although unproven, this may represent extreme distortion of elastic lung architecture.

Acceleration atelectasis is a well-known phenomenon which occurs with +Gz exposure while breathing high concentrations of inspired oxygen (15). It is caused by closure of small airways at the lung bases because of the increased +Gz, with resorption of oxygen from the airspaces distal to the closed airways.

Gravitational forces acting on the lung within the thorax cause a gradient for pleural pressure increasing down the lung, the result of which is a gradient for ventilation distribution with dependent areas (lung bases) receiving more ventilation than lung apices under normal tidal breathing. Lung perfusion is likewise affected by gravitational forces, with a gradient for lung perfusion increasing from apex to base. Even under normal +1Gz conditions, the

gravitational-induced gradients cause a mismatch of ventilation and perfusion with arterial hypoxemia due to the venous admixture. Increasing gravitational-inertial forces accentuate this ventilation-perfusion mismatch (16), with increasing venous admixture and hypoxemia. Atelectasis occurring in dependent lung zones produces right to left shunting and hypoxemia which is not corrected by positive-pressure breathing.

It is likely that the lung is the limiting factor in man's ability to withstand gravitational-inertial forces. There remains an unanswered question as to whether repeated exposure to high sustained G-forces may permanently affect lung structure and function. There is at least one report of lung dysfunction in fighter aircrew compared with a control group of transport pilots (17). This concern needs to be addressed by further research.

Lung diseases which cause pulmonary dysfunction under normal conditions such as small airways disease will only exacerbate the problems occurring in the flight environment. Diseases which disrupt lung architecture such as emphysema, cysts and bullae make the lung more susceptible to rupture under increased gravitational forces. Aircrew candidates should be carefully screened for respiratory disease and small airways dysfunction, and periodic screening of trained aircrew should include screening for respiratory diseases. The papers by Air Commodore Hull and Commander Gray address these concerns.

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	HIST/PHYS	ECG	EX ECG	LIPIDS	PFTs	CXR	ECHO
BELGIUM	6M	1Y	NR	2Y	1Y	1Y	NR
CANADA	2Y short/alt	<40 4Y >40 2Y	NR	<40 4Y >40 2Y	NR	NR	NR
DENMARK	<40 1Y >40 6M	<40 1Y >40 6M	NR	<40 1Y >40 6M	<40 1Y >40 6M	NR	NR
FRANCE	6M	1Y	NR	5Y	NR	NR	NR
GERMANY	1Y	1Y	1Y	1Y	1Y	1Y	NR
GREECE	6M	1Y	>40 2Y	1Y	1Y	1Y	NR
ITALY	1Y	1Y	1Y	1Y	1Y	1Y	NR
NETHERLANDS	6M/1Y	6M/1Y	NR	6M/1Y	6M/1Y	NR	NR
NORWAY	<40 1Y >40 6M	<40 1Y >40 6M	<40 6Y >40 3Y	<40 1Y >40 6M	<40 1Y >40 6M	NR	NR
PORTUGAL	1Y	1Y	1Y	>40	NR	1Y	NR
USAF	2Y short/alt	NS	NR	NS	NS	NR	NR
US ARMY	1Y	1Y	1Y	NR	NR	NR	NR
US NAVY	<40 3Y >40 1Y	<40 3Y >40 1Y	NR	1Y	NR	<40 3Y >40 1Y	NR
UK/RAF	1Y	25,30 >30 2Y >40 1Y	NR	25,30 >30 1Y >40 2Y	1Y	NR	NR

NR - Not Routine. Done when indicated clinically

NS - Not specified

PFTs - Pulmonary Function Tests

CXR - Chest x-ray

6M - six monthly

1Y /2Y/3Y - every 1,2,3 years respectively

Table 6. Frequency of cardiopulmonary screening

## SCREENING FOR ASYMPTOMATIC CORONARY HEART DISEASE

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### SUMMARY:

Predicting the presence of coronary heart disease in an asymptomatic population is a very difficult task. Because of the possible sudden and incapacitating presentation of coronary heart disease and its common occurrence in industrialized nations, screening for this disorder is an important aeromedical concern. Nonsignificant disease can lead to coronary events and is also likely to progress to significant disease. Also, lifestyle changes and other interventions may affect the progress of insignificant disease. Screening efforts in the military aviator population should therefore be aimed at detecting any measurable degree of disease. This review will discuss problems inherent to screening an asymptomatic population, different screening tests and risk stratified approaches to screening for coronary heart disease.

### 1. INTRODUCTION:

Screening for coronary heart disease (CHD) is a very prominent aeromedical issue. Screening is testing for a disease in patients who have no clinical evidence for that disorder. Typically, screening is not warranted unless early detection leads to therapy that can change the future prognosis of that disorder, i.e. reduce mortality or morbidity. For aerospace medicine, screening is also warranted occupationally to identify diseases before clinical presentation if that presentation may be sudden and unexpected, jeopardizing the aviator, other aircrew or mission completion. Screening tests for CHD have classically targeted clinically significant CHD, defined as 50% or greater coronary artery diameter reduction. Lesions of this degree are considered capable of causing ischemia and our usual diagnostic tests are designed to detect ischemia. However, we have a need to detect earlier degrees of CHD. We cannot wait for significant disease to develop and manifest itself clinically in the military aviation arena. Less significant disease will likely progress and later develop symptoms or other events. And less than 50% lesions are quite capable of plaque rupture and subsequent clinical events. Also, preventive efforts and lesion regression could be expected to be more effective if implemented earlier in CHD development.

Our problem with screening for CHD in the military aviator population revolves around the low prevalence of CHD in this group. Even for the detection of significant CHD, our classic tests, such as exercise testing, function poorly in this population. Sensitivity is the ability of a test to detect those with disease (true positives divided by true positives plus false negatives). Specificity is the ability to correctly label those without disease (true negatives divided by true negatives plus false positives). Sensitivity and

specificity are considered characteristics of a given test and unaffected by disease prevalence in the population tested. Predictive value is very much dependent on disease prevalence in the population tested. Positive predictive value is the percentage of patients with a positive test who actually have the disease (true positives divided by all positives) and negative predictive value is the percentage of patients with a normal test who actually do not have the disease (true negatives divided by all negatives). In the 1987 AGARD Short Course on Cardiopulmonary Aspects of Aerospace Medicine, Hickman (1) gave an excellent, in depth discussion of this problem which will briefly be reviewed. He used the example of a test with sensitivity 60% and specificity 90% in a population of 20,000 subjects with disease prevalence 50%. There will be 6,000 true positive tests out of 7,000 total positive tests for a positive predictive value of  $6,000/7,000 = 85.7\%$ . If we change only the prevalence to 5%, then there will be 600 true positive tests out of 2500 total positive tests, yielding a positive predictive value of only  $600/2500 = 24\%$ . Thus, the positive predictive value of even an excellent test will be seriously affected by disease prevalence. The military aviator population probably has a CHD prevalence of about 5% or slightly less, certainly no more than 10%. Our efforts to screen for CHD must therefore consider this problem of disease prevalence and predictive value of our tests. We will discuss some different modalities of testing before continuing to address this problem.

### 2. RESTING ELECTROCARDIOGRAM:

Normal subjects without angiographic disease may have significant changes on electrocardiogram (ECG). On the other hand, a significant percentage of angiographic abnormalities may be found in asymptomatic aircrew with ECG abnormalities(2). Frequency of ECG changes increases with age as does the incidence of CHD, complicating the use of ECG to screen for CHD. The American College of Cardiology/American Heart Association (ACC/AHA) Task Force (2) recommended an initial screening ECG as a Class I indication in patients of any age who are in special occupations such as pilots. Class I indications are those in which there was general agreement that ECG was useful. Follow-up ECGs as a Class I indication in asymptomatic subjects were only recommended in those individuals over the age of 40. The USAF follows a similar policy. Screening ECG is performed prior to flying training to exclude such disorders as bundle branch block, pre-excitation, etc. Repeat routine ECG is not performed until age 35 due to the low yield of follow-up ECGs. Sox (3) reviewed 40 articles to address the utility of screening ECG. He concluded that screening ECGs should not be done in asymptomatic men without evidence of cardiac

disease or risk factors. Presence of Q waves or nonspecific ST/T wave changes (NSSTTWCs) is associated with increased mortality from CHD with a relative risk up to 4.6. However, many people without angiographic disease have resting ECG changes and many people with angiographic disease have normal resting ECGs. Due to the low prevalence of ECG changes and CHD in a healthy population, these ECG changes are poor predictors of CHD. In a review by Mirvis (4), he quoted average prevalence rates for NSSTTWCs of 8.1% and 8.5% in men and 7.7% and 12.3% in women with prevalence increasing with age. In a large series of angiographic cases at his institution 9801 patients underwent coronary angiography. 44.3% had resting NSSTTWCs - of these, 25.6% had no CHD and an additional 17.9% had only lesions less than 70%. Again, resting ECG is a poor screening test for CHD.

### 3. EXERCISE TESTING:

Exercise testing by ergometry or treadmill is probably the most common screening test after history/physical examination and resting ECG. The ACC/AHA Task Force (5) reviewed exercise testing and concluded that there were no class I indications for screening exercise testing of asymptomatic individuals. Class I indicates conditions for which there is general agreement that exercise testing is justified. Class II indicates conditions for which exercise testing is frequently used but opinion is divergent regarding value and appropriateness. Class II recommendations included asymptomatic men over age forty in special occupations or with 2 or more CHD risk factors. Ten studies were reviewed that followed CHD endpoints after exercise testing. Positive predictive value ranged from 5.46%, most were less than 25% and the average predictive value was 21%. Average sensitivity was 50% and specificity 90%. Angiography in these and other similar studies confirm the low predictive value of screening exercise tests in asymptomatic patients. Sox (6) also reviewed this subject and found no evidence that screening exercise tests resulted in prolonged life or improved quality of life. The cost-effectiveness of a screening exercise test in patients with CHD risk factors was comparable to accepted practices such as the screening and treatment of hypertension; without risk factors it was not cost effective. In a review of coronary artery fluoroscopy results in USAF aviators undergoing coronary angiography for aeromedical indications, Loecker (7) reported positive and negative predictive values of the accompanying exercise tests of 33% and 65%, respectively. Also in USAF aviators undergoing angiography, Hickman (1) reported a positive predictive value of 10% for unstratified exercise testing and 25% for exercise testing done in individuals with serial NSSTTWCs on resting ECG. This was in detecting lesions of 50% or greater. From a review of the literature, Froelicher (8,9) reported a positive predictive value of 6% for hard clinical endpoints and 26% if angina was included as an endpoint. He repeated the point that the problem of diagnosing CHD after an exercise test depends on the patient population characteristics and sensitivity/specificity.

Sensitivity and specificity may be affected by the population tested, but usually are not due to patient mix. In a low prevalence population sensitivity and specificity may be different from values classically reported. In USAF aviators he found a predictive value of 20% for CHD endpoints, including angina. These and other articles (10,11) do show that screening exercise tests are an independent predictor of CHD, sometimes only in asymptomatic patients with CHD risk factors. However, although they demonstrate statistically significant results, all are plagued with low positive predictive values due to low disease prevalence. Two angiographic studies from the USAF (7,12) documented a prevalence of 17% for lesions 50% or greater and a prevalence of 33% for any measurable disease (10% or greater lesion). This is a select population undergoing angiography. The prevalence of CHD in the general military aviator population would be certainly 10% or less, probably 5% or slightly less. Because of the low predictive value of screening exercise testing, too many normals would be subjected to further testing, including procedures with measurable risk. A better method to identify asymptomatic CHD in our aviators is much needed.

### 4. OTHER CHD SCREENING METHODS:

Schwartz (12) reported thallium-201 (TI-201) scintigraphy results in 845 USAF aviators undergoing aeromedical coronary angiography. Six risk subgroups were defined by age (less than 45 versus 45 or greater) and by the ratio of total cholesterol to high density lipoprotein (HDL) cholesterol (less than 4.5, 4.5 to 6.0, greater than 6.0). Results were reported for defining CHD with coronary artery lesions of 50% or greater. Sensitivity/specificity were 45%/78% across all risk subgroups, much lower than reported in clinical populations. The prevalence of disease as defined above was 16.9%. Predictive values varied across risk subgroups. Positive predictive value was 8-43% and negative predictive value was 81-97%. Normal TI201 indicated a low risk of CHD but an abnormal TI-201 was likely to represent a false-positive result. In his report of coronary artery fluoroscopy, Loecker (7) also reported results of the accompanying TI-201 scintigrams. Positive predictive value was 35% and negative predictive value was 74% for detecting any measurable lesion 10% or greater. The utility of TI-201 scintigraphy as a screening procedure is limited similar to exercise testing. Its greater cost makes it even less appealing.

Other imaging modalities that test for ischemia are also unsatisfactory for use in screening asymptomatic individuals for CHD. Although they may have improved results over exercise testing in a clinical population, they will suffer from the same poor predictive values, again due to the low prevalence of CHD in our military aviator population. Increased cost would also make them very unappealing as screening tests. Stress echocardiography is a valuable clinical tool but there are no large studies of this procedure in a population similar to military aviators. Stress echocardiography also has a problem with false negative studies in single vessel and mild-moderate

disease, both of which are of significant aeromedical interest. Other considerations include scintigraphy with radionuclides other than thallium and positron emission tomography. These various imaging modalities are helpful and appropriate as secondary and tertiary level testing procedures but not for screening.

#### 5. CORONARY ARTERY CALCIFICATIONS:

Fluoroscopy for coronary artery calcifications is a promising procedure which is readily available, inexpensive and low risk. It is an older noninvasive method which has not been used in clinical populations because it does little to predict prognosis or disease severity. Also, the incidence of coronary artery calcifications not related to obstructive lesions increases with age. It is an anatomic test, however, which detects abnormalities in the vessel wall rather than consequences of a lesion severe enough to reduce flow through the vessel. As such it may be of use in screening for any measurable CHD (lesions 10% or greater) which are considered aeromedically significant. Unfortunately much of the older literature regarding coronary artery fluoroscopy (CAF) only reports results for significant CHD (lesions 50% or greater). Loecker (7) reported CAF results in 613 USAF aviators undergoing aeromedical coronary angiography. Sensitivity/specificity were 66.3%/77.6% for significant CHD and 60.6%/85.9% for measurable CHD. Positive predictive value was only 37.7% for significant CHD, but was 68.9 for measurable CHD. Negative predictive value for the two categories of CHD was 91.9% and 80.9%, respectively. CAF was much more successful to predict any degree of CHD than to predict severity of disease. A negative CAF predicted low risk of any measurable CHD while positive CAF significantly increased the likelihood of CHD. The US Army (13) also uses CAF for second level screening in their aviators with a positive predictive value of 45.8% for significant CHD and 83.1% for any measurable CHD. Digital subtraction fluoroscopy has also been investigated. Detrano (14) reported a sensitivity/specificity of 83%/79% for this method in detecting any measurable CHD in 191 asymptomatic individuals undergoing coronary angiography. Standard CAF was less sensitive but more specific (fewer false positives) in the same patients. Fast/ultrafast computed tomography (CT) has also been used to detect coronary calcification with improved sensitivity over fluoroscopy but some loss of specificity. Most populations include a mix of symptomatic and asymptomatic patients with significant and nonsignificant CHD. Kumar (15) reported on 101 patients with normal coronary arteries or lesions less than 50% only. For the detection of moderate CHD only, sensitivity/specificity was 64%/74% for fast CT; a lower sensitivity than generally reported. CAF is superior to rest ECG, exercise testing and other methods in screening for any measurable CHD. Fast CT and digital subtraction fluoroscopy have superior sensitivity compared to CAF. However, these methods are more costly and

less readily available to every aerospace medicine practitioner. CAF is more available, inexpensive and easily performed. Accuracy does depend on the experience of the operator, however.

#### 6. RISK STRATIFIED APPROACH TO CHD SCREENING:

Our aim in military aerospace medicine is to screen for CHD to identify angiographic disease now, rather than to predict future events. Hopefully, identification of disease will also lead to risk factor modification and other interventions that will favorably affect future events. Detrano (14) presented an excellent review of CHD screening strategies similar to this paper. He made a strong argument for a goal of identifying CHD at the subclinical level (any measurable CHD) rather than only significant CHD. The ability to affect long term prognosis and the unique concerns for certain occupations such as aviators strongly favor such a goal. Detrano (14) proposed testing for coronary artery calcification as a modality uniquely suited for detecting anatomic disease. Other available testing procedures assess for lesions severe enough to cause ischemia. He finally proposed a combination of exercise testing and a screen for coronary artery calcification as an approach to CHD screening. However, all tests will be subject to the problem of low CHD prevalence and low predictive value in our military aviator population. Therefore, some risk stratification must be done before screening tests are performed. This will select out a subpopulation at higher risk of CHD with a greater prevalence of disease. This would decrease the number of people without CHD who are subjected to screening, improve predictive accuracy and decrease the number of false positive tests.

All of the above discussed test results occurred in patient populations that were stratified in some fashion, particularly studies with angiographic data. Open screening was not performed in total populations; the populations were preselected. We would expect even less helpful results in the entire population of asymptomatic subjects. Hickman (1) reported a 10% positive predictive value for an abnormal exercise test performed in all aviators over the age of 37. This was an unstratified group except for age. By performing treadmills only in those with serial NSSTWCs, positive predictive value increased to 25%. Retrospectively stratifying by the number of associated classic risk factors increased the positive predictive value progressively from 9% with no risk factors up to 64% with four risk factors. Uhl (16) also reported similar data in USAF aviators stratified by the ratio of total cholesterol to HDL cholesterol. In a series of aviators undergoing angiography for an abnormal treadmill, 64% of those with a ratio greater than 6.0 had CHD while only 2% of those with a ratio less than 6.0 had CHD. In a report on TI-201 scintigraphy in USAF aviators, Schwartz (12) retrospectively stratified the subjects by age (less than 45 years versus 45 years or older) and total cholesterol to HDL cholesterol ratio (less than 4.5, 4.5-6.0, greater than 6.0). Positive predictive value for an abnormal TI-201 scintigram

ranged from 8% for age less than 45 and ratio less than 4.5 up to 41% for age 45 or older and ratio greater than 6.0. All this USAF data applied to identifying significant CHD of 50% or greater lesions rather than any measurable disease.

These considerations emphasize the importance of stratifying our military aviator population to preselect a smaller subpopulation with a higher prevalence of CHD for further screening tests. A systematic stratification approach would involve parameters readily obtained on routine flight examinations. Initial screening tests after stratification should be relatively inexpensive and available. A number of stratification schemes have been reported in the literature; the Framingham risk index is one of the most familiar and widely recognized. Two other strategies will be discussed.

In the 1987 Short Course on Cardiopulmonary Aspects of Aerospace Medicine, Hickman (1) introduced the USAF School of Aerospace Medicine risk index (RI). The RI is a dimensionless number designed to express risk of angiographic disease rather than risk of future events. It was derived retrospectively from angiographic data in USAF aviators with an average age of 40 years. RI equals total minus HDL cholesterol, that sum divided by age squared.  $RI = (TC - HDL)/(AGE^2)$ . Such risk factors as family history, smoking, hypertension and diabetes do not enter into the RI. In analyzing the data to derive the RI, 90% of the predictive information was contained in age and total and HDL cholesterol. As a rule, USAF aviators do not have diabetes or untreated hypertension and family history is less helpful in this relatively young population. And the effects of smoking are partly expressed in lipid profile and age. In the derivation of the RI, positive predictive value of an abnormal treadmill for significant CHD was only 5.7% in the lowest risk group and increased progressively to 75% in the highest risk group. In 1987, the RI was just entering a prospective validation phase. Details of the implementation plan were previously reported by Hickman (1). Since then 75 aviators were referred to Brooks Air Force Base for further evaluation for elevated RI and/or abnormal local treadmill test prompted by an elevated RI (17). Of these 75 cases, 34 underwent coronary angiography and 11 (33%) had measurable CHD. Ten of the 11 had 30% or greater lesions. Five of the 11 with CHD had normal treadmill and Tl-201 testing; they were identified by CAF alone and all 5 had 30% or greater lesions. This represented a significant improvement over prior CHD detection efforts. Unfortunately, progress on the validation was postponed for administrative reasons and no further data is available beyond these promising small numbers at this time.

The US Army uses a different stratification method in their aviators (13). Initial stratification is done with data from the annual flight physical examination. Acceptable parameters are a Framingham risk index less than 5%, total cholesterol less than 270 mg/dL (7.0 mmol/L), and total/HDL cholesterol ratio less than

6.0. If an aviator exceeds any of these three parameters, screening treadmill and CAF are performed locally. An abnormal treadmill or CAF prompts further evaluation, usually including coronary angiography. As of Oct 92, over 1800 aviators failed initial stratification and 224 had an abnormal treadmill or CAF. Angiography was performed in 177 of these 224. The positive predictive value for any measurable CHD was 83.1% for CAF and 52.5% for treadmill. For significant CHD, the positive predictive value was 45.8% for CAF and 31.9% for treadmill. The positive predictive value of both CAF and treadmill was improved by stratification before screening tests were done.

These several examples are not intended to endorse any particular method. Their superior results do demonstrate that we must use some stratification process to preselect those higher risk military aviators that should be subjected to initial screening tests. From the data presented, a screen for coronary artery calcification seems to be the most successful screening test with CAF being the most practical method presently available. A combination of exercise testing and fluoroscopy as used by the US Army (13) is a very prudent approach. Detrano (14) recommended a similar approach of exercise testing and digital subtraction fluoroscopy. For reasons previously discussed, our search for CHD in the military aviator should be for any measurable CHD, not just for significant CHD. This strategy of stratification followed by screening tests has a very good yield for this search.

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## AEROMEDICAL DISPOSITION FOR CORONARY ARTERY DISEASE

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### SUMMARY:

Coronary artery disease continues to be a significant concern in aerospace medicine. Coronary disease is a major cause of deaths and sudden incapacitation for males in the flying age population. When coronary disease is found in an aviator, the benefits of his remaining on flying duties must be weighed against his risk of an incapacitating event. The following chapter reviews the probability of a cardiac event in populations of varying degrees of coronary disease including patients following myocardial infarction, angioplasty, and coronary artery bypass surgery. The U.S. Air Force (USAF) experience and recommendation for flying waivers will also be discussed.

### INTRODUCTION:

Coronary disease remains asymptomatic in all individuals for a variable length of time. The initial symptom will then be angina (either stable or unstable), myocardial infarction, or sudden death. Based on mortality rates for ischemic heart disease in the United States from the "Monthly Vital Statistics Report", National Center for Health Statistics, Washington DC, (1) the annual death rate per 100,000 population for white males age 45 through 54, was 266.9 or 0.27% per year. For the age group 55 through 64, this increased to 715.1 or 0.72% per year. The annual incidence rates for myocardial infarction and angina from the Framingham study for males ages 45 through 54 was 0.7% per year (2). Although this overall rate seems low, any nation with a large pilot population should expect several cardiac events each year. Since coronary artery disease may remain asymptomatic for an extended period of time and then present with an unpredicted catastrophic and incapacitating event, there is a clear cut need to identify individuals with coronary artery disease before this first symptom occurs. This need has led to various screening strategies that have been previously discussed. Once coronary disease has been identified, a rational approach should be pursued in order to determine the possibility of continued flying duties, the degree of restrictions necessary on flying duties, and the type and frequency of medical follow-up.

### NORMAL CORONARY ARTERIES:

In order to determine a rational approach to the aeromedical dispositions for coronary artery disease, the natural history of this disease should be examined. Although coronary angiography has many significant limitations, it remains the most accurate method for

diagnosing coronary atherosclerosis in a living subject. Because of this, all long-term epidemiologic studies that examine the natural history of coronary artery disease subdivide their population based on the findings of arteriography. Although many factors other than the degree of coronary stenosis are predictive of prognosis, the degree of coronary narrowing is generally used as the basis of all other analyses. One of the first large angiography follow-up studies was published by Bruschke et al. in 1973 (3). A series of 500 patients with normal angiography or mild coronary artery disease were followed for 5 years. Three hundred forty-two patients had normal coronary angiograms. In this group, two (0.6%) had presumed cardiac deaths and three (0.9%) had acute myocardial infarctions within 5 years. Using the mortality tables for the 1967 United States Vital Statistics, the expected 5 year mortality rate from atherosclerotic heart disease in a population matched for age and sex with this angiographically normal group was 1.1%. Even though most individuals underwent cardiac catheterization for indications such as chest pain, this angiographically normal group had a cardiac mortality that was more favorable than the unscreened general U.S. population. The same group followed to 10 years with data on 357 patients felt to have normal coronary angiograms was still very favorable with a cardiac mortality of 0.8%.

A similar study was published by Kemp et al. using the data from the CASS Registry. Patients in the CASS Registry (4) also underwent coronary angiography because of suspected coronary artery disease. Of the 21,487 consecutive coronary angiograms taken from multiple clinical sites, 3,136 angiograms were felt to be completely normal. Cardiac deaths occurred in 14 individuals (0.45%) after 7 years of follow-up. This study also confirms the earlier findings by Bruschke that normal coronary angiography is very predictive of an excellent prognosis over 5 to 10 years. In view of these findings, aviators found to have normal coronary angiography are returned to unlimited flying duties. Although the indications for angiography may be chest pain or abnormal non invasive testing suggesting cardiac ischemia, we believe in the face of normal angiography these symptoms or test findings are nonspecific and not indicative of small vessel disease or other cardiac pathology that could adversely affect prognosis or flying safety.

### MILD CORONARY ARTERY DISEASE:

Once coronary artery disease is identified, the prognosis is significantly affected. Bruschke et al. followed 101 patients with mild coronary lesions

defined as a luminal narrowing of less than 30% (3). This group had a 2.0% cardiac mortality over 5 years with a predicted cardiac mortality of 2.2% based on the 1967 Table of Vital Statistics. However, in 57 patients with a maximum lesion of 30% to less than 50%, the 5 year rate for cardiac mortality and myocardial infarction was 5.3% and 3.5%, respectively. The predicted 5 year cardiac mortality for this group was only 2.1%. Bruschke therefore showed an increased cardiac mortality over the unscreened general population for patients with coronary artery lesions of 30% to less than 50% narrowing. This trend was confirmed in their 10 year follow-up series showing coronary events including death, angina, subsequent myocardial infarction and angiographic evidence of progression of coronary obstruction in 13.8% in the less than 30% group. The coronary event rate was 33% in the 30% to less than 50% coronary lesion group.

The CASS Registry study showed a more favorable trend in their group with mild coronary artery disease. In 915 individuals followed with mild coronary disease (less than 50% stenosis in one or more segments) Kemp et al. found 18 (1.97%) cardiac deaths over 7 years (4).

#### MINIMAL CORONARY ARTERY DISEASE STUDY GROUP:

Because of the favorable prognosis for individuals with mild coronary disease demonstrated by Bruschke et al. in the early 1970s, the U.S. Air Force (USAF) initiated the Minimal Coronary Artery Disease (MCAD) study group. This group was established in 1976 in order to allow waivers for aviators with MCAD to return to restricted flying duties. This study group also created a mechanism to follow individuals with MCAD to establish the prognosis for this population. This study group also provided the required clinical follow-up for aviators with CAD. The angiographic criteria called for a single lesion of 30% or less. Since the prognosis for an individual with diffuse coronary atherosclerosis is felt to be worse than an individual with few lesions, an additional criteria termed "aggregate" was added to the angiographic criteria. This restricted individuals with multiple lesions by using a simple technique of adding the numerical sum of all separate lesions. Individuals with an aggregate sum of greater than 50% were disqualified from flying duties. Other entry exclusions included left main coronary disease, symptoms consistent with ischemia, evidence of a prior myocardial infarction, any tachyarrhythmia, significant conduction defects such as left bundle branch block, right bundle branch block, Wolff-Parkinson-White Pattern, and any valvular heart disease. Aviators in this study were seen on an annual basis and repeat cardiac catheterizations were performed at 3 year intervals. This was felt appropriate since the likelihood of identifying coronary disease progressing past 30% was unlikely using standard non invasive tests such as treadmill testing and later thallium scanning.

By 1990, 116 individuals with MCAD were evaluated with a mean follow-up of 5.1 years. Follow-up was obtained in 100% of these aviators. No deaths occurred in this group. One individual developed angina 9 years after cardiac catheterization. There were no myocardial infarctions reported. Repeat angiography was performed in 22 aviators. Five individuals were noted to have progression by repeat angiography. One aviator underwent coronary angiography just prior to two years for clinical reasons. Although his maximum lesion remained 30%, he exceeded the aggregate sum of 50% because of progression at a previously normal site. At 3 years, one person progressed from a 20% lesion to 70% and a second person progressed from 20% to a total occlusion of a large obtuse marginal branch. At 6 years, one person progressed from 20% to 40% and a second from 25% to 60%.

Prior to initiating the MCAD protocol in 1976, 24 aviators had been disqualified because of the presence of MCAD on cardiac catheterization.

The mean follow-up in this group was 14.9 years. There were no deaths reported but four individuals had myocardial infarctions and a fifth developed angina. Myocardial infarctions occurred at 6, 8, 9 and 10 years after angiography and angina occurred 7 years after angiography in the fifth individual. A review of classic risk factors did not predict those having cardiac events.

The third group to be evaluated during this review included everyone with a maximum lesion of 30% or less, but with an aggregate sum of all lesions exceeding 50%. This group consisted of 21 aviators. The maximum aggregate score was 105%. This occurred in an individual with a chest pain syndrome suggesting coronary artery spasm. Of the 20 asymptomatic individuals, the maximum aggregate score was 100%. Two aviators developed endpoints of angina both at 13 years after cardiac catheterization.

Endpoints Occurring By 10 Years of Follow-Up	
<50% Group	50% Group
Unstable angina at 1 yr	Angina at 1 yr
Progression to significant lesion at 6 yr	Angina at 1 yr
	Angina at 2 yr
	Angina at 2 yr 1 mo
	Angina at 3 yr
	MI at 3 yr 2 mo
	MI at 4 yr
	Progression at 4 yr
	Progression to 75% with atypical chest pain at 5 yr 5 mo
	Angina at 6 yr 4 mo
	MI at 6 yr 5 mo

Table 1.

This review of MCAD confirmed our initial impression that aviators with coronary lesions of 30% or less had an acceptable prognosis that would justify continued flying duties. Although cardiac events began 5.6 years after angiography and two aviators developed progression to significant coronary artery narrowing by 3 years after angiography, the U.S. Air Force waiver policy remained intact. The restriction on aggregate score was increased to 100% since this was the limit of our experience in asymptomatic individuals.

#### MODERATE CORONARY ARTERY DISEASE:

Following examination of the MCAD group, the moderate CAD group was reviewed. The definition of moderate CAD for this study was a maximum lesion from 31% to 50%. The angiographic criteria were met by 104 patients, but 12 were excluded for several reasons such as a prior myocardial infarction, follow-up therapy with coronary angioplasty, left ventricular wall motion abnormalities, and other miscellaneous reasons. Follow-up was obtained in 99% of individuals or their spouse. One individual could not be contacted, but accurate follow-up of 9 years was available. A total of 92 male subjects were seen at an average age of 45.6 years with a mean follow-up of 8.5 years. This group was subsequently divided into 38 aviators with lesions of 31% to less than 50% and 54 aviators with a maximum lesion of 50%. Average age and mean follow-up were comparable in these two groups. Cardiac endpoints occurring prior to 10 years were examined in both groups. In the less than 50% group, two endpoints occurred. Unstable angina developed at one year and progression to a significant coronary lesion by cardiac catheterization occurred at 6 years. In the 50% group, 10 individuals developed cardiac endpoints as listed in Table 1. This included angina developing in two aviators at one year postcatheterization and a myocardial infarction occurring at 3 years postcatheterization. One individual later died after initially presenting with a myocardial infarction. In the less than 50% group, the 5 and 10 year cardiac mortality was 0%. In the 50% group, the 5 to 10 year mortality was 2.1% and 3.3%, respectively. In the less than 50% group, the annual cardiac event rate at 5 and 10 years was 0.6% and 0.4%, respectively. In the 50% group, the annual cardiac event rate at 5 and 10 years was 2.9% and 2.3%, respectively.

Analysis of all cardiac risk factors showed family history to be the only significant predictor of a cardiac event in either group. Four endpoints occurred in subjects taking aspirin. These events were stable angina in two and progression of coronary disease in two. Six endpoints occurred in subjects not taking aspirin. These included three with myocardial infarction and one with unstable angina. Although the numbers are too small to be statistically significant, there is a trend towards an acute presentation in those individuals not taking aspirin. Although the aggregate score did not appear to be predictive in the MCAD group, endpoints occurred in the less than 50% group only in individuals with an initial aggregate score of 160 or greater.

The final recommendation following this review was to increase criteria for the MCAD study group to allow waivers for individuals with a maximum of a 40% narrowing in any one artery and an aggregate score of 120% or less. Using this criteria, the first cardiac event occurred at 10 years 3 months. Based on an annual cardiac event rate of 2.9% for the 50% coronary lesion group, waivers were felt to be inappropriate for this population.

#### SIGNIFICANT CORONARY ARTERY DISEASE:

The medical literature also supports an increased coronary event rate for patients with lesions of 50% or more. An early article by Bruschke et al (5) from 1973 followed 590 consecutive non surgical cases with 50% or more lesions for 5 to 9 years. Nearly all patients were referred because of chest pain, but a small minority had a history of congestive-heart failure as the primary indication for the study. There were 527 men (mean age 49.4 years) and 63 women (mean age 52.5 years). The five year cardiac mortality for the entire group was 34.4% with a 15.6% mortality for patients with one vessel disease, 37.8% for patients with two vessel disease, and 53.8% for patients with three vessel disease. There was also a 56.8% five year mortality for patients with at least 50% narrowing of the left main coronary artery.

The survival of medically treated patients in the CASS Registry published in 1982 showed a somewhat better prognosis for patients with significant coronary artery disease (6). The criteria for clinically significant coronary disease in the CASS study was either 70% or more obstruction of the right coronary artery, left anterior descending artery, or circumflex artery or 50% reduction in the internal diameter of the left main coronary artery. The four year survival rates for patients with one, two, and three vessel disease was 92%, 84% and 68%, respectively. In patients with three vessel disease and left main coronary artery disease survival was decreased to 60% at four years.

In addition to the amount of coronary artery disease present, left ventricular ejection fraction was also found in this study to be predictive of prognosis. Patients with at least one vessel disease excluding the left main coronary artery and an ejection fraction from 50% to 100%, 35% to 49%, and less than 35% had four year survivals of 92%, 83%, and 58%, respectively. Within each subgroup of patients with one, two, and three vessel disease, the ejection fraction was also an important predictor of survival.

Even though the survival rate for the CASS study appears to be better than previously published studies, the CASS data demonstrates a 5% four year mortality for single vessel disease with normal left ventricular function. This represents the sub population with the most favorable mortality statistics. In addition, this only represents overall mortality and does not reflect episodes of myocardial infarction, angina, or other incapacitating events. Although a specific cutoff for

cardiac events and continued flying duties have not been set, we believe that the event rate for individuals with coronary - lesions of 50% or greater exceeds a reasonable event rate for individuals recommended for continued flying duties.

#### MYOCARDIAL INFARCTION:

A myocardial infarction further complicates the course of coronary artery disease. Multiple studies examine the long-term prognosis of this population. The prognosis of post infarction patients with persistent angina or significant impairment of left ventricular function will not be considered in this discussion since their aeromedical disposition is obvious. The disposition of asymptomatic stable post infarction individuals is more difficult. The CASS randomized trial examined the 5 year prognosis of asymptomatic post infarction patients.

As a group, the asymptomatic post infarction patients should be expected to have a more favorable outcome than their symptomatic counterparts. A report from the CASS study examined the 5 year survival of 160 asymptomatic post infarction patients (7). The 5 year survival of the medically and surgically treated groups was 88% and 89%, respectively. The probability of remaining alive without a recurrent myocardial infarction, however, was 78% and 80% for the medical and surgically treated groups, respectively. There was also another 19 subjects from the medically treated group who required bypass surgery during this 5 year period. These numbers do not include additional subjects that developed angina or other symptoms that did not require operative therapy.

A second study examining a similar group of asymptomatic post infarction patients was reported by Proudfit et al (8). This population was similar to the group reported in the CASS Registry. However, all subjects with a myocardial infarction and left main coronary artery stenosis were excluded from this report. Survival in this population was 85.4% at 5 years and approximately 75% at 8 years. Bypass surgery was required in 14% by 5 years and 17% by 8 years. Although all cardiac events were not listed, they examined the "failure of medical treatment" (defined as death from cardiac caused, coronary surgery, or myocardial infarction) in this population. Failure of medical treatment was listed at 33.6% during the 5 year follow-up. This also does not include other symptoms of coronary artery disease that failed to produce a myocardial infarction or require coronary artery bypass surgery.

A population that would most likely be considered for a return to flying duties post myocardial infarction are those individuals found to have only minimal coronary artery disease after infarction. A group of such patients was studied by Kereiakes (9) as part of the Thrombolysis and Angioplasty in Myocardial Infarction study group [TAMI]. A group of 799 patients successfully treated with intravenous thrombolytic therapy for an acute myocardial infarction were studied. Forty-three patients (5.5%)

were found to have a residual obstruction of  $\leq 50\%$  90 minutes after thrombolytic therapy. An additional 42 patients (5.4%) had a less than 50% stenosis on angiography during the follow-up studies 7 to 10 days later. Average follow-up in this group was only 1.5 years, but the mortality was 2.4%. Reinfarction occurred in 5%. This study compared the prognosis of individuals following myocardial infarction with minimal residual stenosis versus significant ( $\geq 50\%$ ) residual stenosis after intravenous thrombolysis. The mortality rate for the  $>50\%$  group was 3.5% and reinfarction rates were identical in both groups. Since additional symptoms of angina and subsequent bypass surgery were not listed, these percentages represent the lower limit of the cardiac events.

These three papers describe post infarction patients that should have a relatively low subsequent cardiac event rate. In spite of that, the rates for mortality, reinfarction, and the need for bypass surgery exceeds a level that seems reasonable for a military flying population. There may be a rare patient with a sufficiently good prognosis to warrant limited flying duties under unusual circumstances, but as a general policy the U.S. Air Force has not recognized post-infarction patients as qualified for continued flying duties.

#### PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY (PTCA):

As previously stated, the degree of coronary artery narrowing present appears to be an excellent indicator for future prognosis. It seems reasonable that a specific percentage of coronary artery narrowing be chosen as a guideline above which flying waivers are not recommended. Using this approach, it seems logical to consider the possibility of a mechanical intervention to reduce the degree of coronary artery narrowing or to improve blood flow past a stenotic lesion. With the advent of percutaneous transluminal coronary angioplasty (PTCA), coronary artery dilatation has become a real option. For physicians practicing aerospace medicine this poses two separate important issues.

The first issue involves the advisability of recommending PTCA for aviators with coronary artery disease exceeding waiverable limits but who fall short of standard clinical guidelines for this procedure. In effect, these pilots would undergo PTCA strictly for occupational reasons. Although there is no absolute or universally accepted approach to this problem, several issues must first be considered. Although coronary artery angioplasty remains a safe and effective clinical procedure, the complication rate remains well above that for standard diagnostic angiography. The major complications associated with PTCA include death, myocardial infarction, coronary artery closure and emergent coronary bypass surgery. A report from the 1985-86 NHLBI PTCA Registry lists the death rate at 1%, the emergency bypass surgery rate at 3.4%, and nonfatal myocardial infarction rate at 4.3% (10). In addition, restenosis of the dilated vessel continues to occur at between 25% and 30% over the first 6 months. This restenosis may proceed to the same degree or

worse than the originally dilated lesion. Although significant improvements have occurred in the technical aspects and experience of the physicians performing this procedure, re-stenosis rates and complication rates remain relatively stagnant. In view of this complication rate, we feel that coronary artery angioplasty for purely occupational reasons seems inappropriate.

The second pertinent issue concerns the return to flying duties for an aviator after successful PTCA performed for strictly clinical reasons.

Under these circumstances, the occupational issues are not immediately pertinent. However, occupational issues become a concern if the patient has a successful PTCA without suffering a significant complication and remains stable over the long term. Although coronary artery restenosis rates remain at approximately 30%, this restenosis usually occurs over the first 6 months following PTCA. If the dilated lesion remains stable over the first 6 months, late restenosis is uncommon. Recurrent symptoms, however, after 6 months are generally a result of progressive native disease. Cequier et al. (11) examined progression of coronary artery disease and restenosis following PTCA. Twelve percent of patients studied 5 months after dilatation showed evidence of progressive disease. Late angiography was performed at a mean of 34 months and showed progression in 36% of patients. There was, however, no relationship between restenosis of a dilated lesion and progression of native disease.

At the present time, the USAF does not recommend a waiver for flying duties for any individuals following PTCA. There is probably a small subset of pilots who undergo PTCA for clinical reasons that have an angiographic result that returns them to a degree of coronary narrowing equivalent to the waiverable guidelines for MCAD. If these individuals remain stable 6 to 12 months after angioplasty, their prognosis is probably equivalent to individuals with MCAD without angioplasty. The number of people who actually improve to this degree is, in fact, very small, and to date we have not reviewed a case following PTCA that met this criteria. Since we have not recommended waivers for pilots following PTCA, we have also avoided the ethical problem of disapproving angioplasty for occupational reasons, but recommending waivers for pilots who seek these procedures independently.

Although PTCA was the first popular non-surgical intervention for coronary artery dilatation, multiple other procedures have appeared during the last 15 years. The major impetus to identify other forms of coronary artery dilatation is to avoid the problem of restenosis. Unfortunately, the complication rate including restenosis for all other devices appears to be nearly as high or in most cases higher than that for PTCA. The newer methods of coronary artery dilatation are also unproven for the long-term. Since these are generally not first-line procedures and many are still considered experimental, we feel that these other procedures would generally be inappropriate for

a flying population. If the complication rate and restenosis rate are found to be significantly less than angioplasty in the future, these procedures would then be reconsidered.

#### CORONARY ARTERY BYPASS SURGERY:

The longest experience with mechanical revascularization, of course, is with coronary artery bypass surgery. Although there has been vast improvement in the technical aspects of coronary artery bypass surgery over the years, there still remains a significant percentage of patients that experience serious morbidity and mortality. We also feel that coronary artery bypass surgery is unjustified for strictly occupational reasons. However, many patients undergo coronary artery bypass surgery and obtain excellent symptomatic relief with complete revascularization. In pilots with a favorable result, the question of a return to flying status must be considered seriously. As with angioplasty, the central issue remains the probability of developing a sudden incapacitating event.

By the time most patients undergo coronary artery bypass surgery, they have diffuse atherosclerosis and have significant symptoms. Coronary artery bypass surgery should be considered a palliative and not curative procedure in these patients. There are, however, a small number of individuals who have very limited coronary atherosclerosis, but still undergo coronary bypass surgery for sound clinical reasons. Chaitman et al. (12) examined a population of individuals from the CASS Registry that could represent a potential flying population. They specifically examined this population in an attempt to evaluate the possibility that airline pilots could return to flying duties after coronary artery bypass surgery. They reviewed a highly selected population from the CASS Registry in order to define their 5 year prognosis. From 10,312 patients in the CASS Registry undergoing coronary artery bypass surgery, they selected 2,226 men who were less than 60 years of age and had no previous history of bypass surgery, congestive heart failure, cancer, or diabetes requiring medications. Any patient developing a myocardial infarction or who was hospitalized for chest pain, congestive heart failure, a rhythm disturbance or stroke within 12 months after surgery was excluded from this population. Follow-up started 12 months after surgery since this was felt to be a reasonable postoperative observation period prior to considering a return to flying status. The 5 year probability of remaining event-free (defined as free of acute coronary insufficiency, myocardial infarction or sudden death) was 92% for the 1,207 men without previous myocardial infarction. The 5 year probability of remaining event-free was 98% for the 122 men who had never smoked and did not have a history of hypertension. Of the 1,119 men with a previous myocardial infarction and a left ventricular contraction score of 5 to 9, the probability of remaining event free was 91%, and 92% for those with a left ventricular score of 10 or greater. (The left ventricular contraction score is a measure of left ventricular wall motion. A

score of 5 represents normal wall motion. An increasing score means impaired wall motion). In this group, mortality rates were similar to that of the age matched U.S. male population when the left ventricular contraction score was 5 to 9 (4.0% versus 4.3%), but was worse when the left ventricular contraction score was 10 or greater (7% versus 4.2%).

This study looks at the late coronary event rate in a very selected subgroup of men undergoing coronary artery by-pass surgery. This group was selected for its excellent initial prognosis. There is a mean cardiac event rate for the group of 2% per year. This still represents an event rate approximately 4 times higher than the general flying population. Their best outcome occurred in the group of nonsmoking, nonhypertensive males with a 5 year probability of remaining event free. Unfortunately, this occurred in only 122 men out of the entire population of 1,196. This obviously represents a very small and highly selected subpopulation.

The USAF continues to deny waivers for individuals with CAD following coronary artery bypass surgery. This appears to be appropriate in the vast majority of cases. There may, however, be a small subpopulation of pilots who have very limited, but symptomatic disease who have excellent revascularization and an uneventful postoperative course. As surgical procedures improve and long-term follow-up becomes better defined, this issue will be given further consideration.

#### DISCUSSION:

As previously stated, this discussion outlines the general approach taken by the U.S. Air Force for individuals with CAD. The nature of military flying increases the likelihood that a sudden incapacitation will result in a catastrophic event. In addition, any unscheduled interruption in a pilot's ability to perform his duties may have operational impact on any extended military operation. Because of this, we have placed a very low threshold on the annual probability of a cardiac event for disqualifying a pilot. Other types of flying environments, including commercial aviation may find a somewhat more lenient approach to medical standards appropriate.

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## PRIMARY PREVENTION OF CORONARY HEART DISEASE

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### SUMMARY:

The primary prevention of coronary heart disease is a very prominent and vigorously discussed topic in the medical literature, especially in the area of appropriate lipid profile management. Secondary preventive efforts in patients with known disease seem to be clearly beneficial, but the literature and opinions vary considerably regarding primary preventive efforts and how the existing data should be applied to other patient population subgroups. Studies demonstrating regression of coronary artery atherosclerotic lesions seem to lend support to the validity of primary prevention. This topic is of major interest to the military aerospace medicine practitioner. Classic risk factors which are most applicable to the military aviator include lipid profile, smoking and regular exercise. These factors will be discussed with pertinent information from the literature, intending to provide a better understanding of the issues and a reasonable approach to this problem.

### 1. INTRODUCTION:

Coronary heart disease (CHD) is a major public health problem in industrialized nations. Studies such as the MONICA Project(1,2) have demonstrated that the incidence of CHD may vary considerably between countries, even on the same continent. However, as a significant etiology of death and disability, it must still be an important health concern for all industrialized nations. Although CHD mortality rates have decreased significantly in the past two decades, it continues to be the most common cause of death overall in men and women in the United States and the most common cause of non traumatic death in young adults. In the United States, CHD accounts for more than 500,000 deaths and 1.25 million myocardial infarctions per year and a health care cost exceeding \$50 billion per year(3). This review will address some of the risk factors of CHD which are most pertinent to military aviation concerns and the issue of primary prevention of CHD by modification of those risk factors.

### 2. AEROMEDICAL IMPORTANCE OF CHD:

The risk of CHD in military aircrew is less than that of the general population due to the younger age of our aircrew and other biases inherent in our selection and retention standards. Although CHD has been documented as the cause of loss of aircrew, passengers and aircraft in both military and civilian mishaps, demonstrating CHD as the cause behind current mishaps is uncommon, particularly in multipilot aircraft. However, our aircrew are certainly not immune to the development of CHD and its consequences, including the potential for sudden

incapacitation or impaired performance due to ischemic and arrhythmic events. An autopsy study of 275 young men (180 were pilots) with a mean age of 28 years revealed that 25% of them had one or more coronary arteries with a 50% or greater lesion(4). Autopsy studies of U.S. casualties from the Korean War and Vietnam have also reported significant coronary disease in young men in their late teens and early twenties (5,6). CHD is reported to be the most common cause of loss of license in commercial aviation in Western Europe (7). This disease process remains a prominent concern for military aviation due to considerations of flying safety, mission completion, and readiness. This concern is not limited to the aerospace medicine field. The topic of the first Bethesda Conference of the American College of Cardiology was standards of fitness in aircrew (8) and the topic of the eighth Bethesda Conference was cardiovascular problems associated with aviation safety( 9).

### 3. CHD RISK FACTORS:

Many factors have been studied and reported in the literature as possibly contributing to CHD risk. Indeed, Hopkins reported in 1981 a survey of 246 suggested risk factors (10). Several have been accepted generally as important CHD risk factors and may be divided into modifiable and non modifiable risk factors. Non modifiable factors include age, gender and family history. Modifiable factors include lipid profile, hypertension, smoking, lack of aerobic exercise, diabetes mellitus and obesity. Issues regarding hypertension are addressed elsewhere in this publication and will not be repeated. Diabetes also will not be separately addressed. Standards for the detection and treatment of diabetes exist apart from its contribution to CHD risk. Although obesity may be an independent contributor to risk, much of its importance is via its effect on other risk factors. This review will focus on smoking, exercise and especially lipids in separate discussions. Certainly a multifactor approach is most appropriate in a program of primary prevention of CHD, as demonstrated in such studies as MRFIT (11,12,13) and the MONICA Project (1,2). In reviews of clinical trials of risk factor modification, an excess of non-CHD deaths is seen in single factor primary cholesterol-lowering trials but not in multifactor intervention trials (14). Unfortunately, most prevention trials address only one factor and control for the others, so there is less information on multifactor efforts.

### 4. LIPID PROFILE:

In both Europe and North America, the most controversial topic regarding risk factor modification for the primary prevention of CHD seems to be the



lipid hypothesis. Epidemiologic studies (migrant studies, in and between population studies), animal experiments and clinical trials all demonstrate a correlation between total cholesterol level and incidence of CHD. There seems to be no threshold for this effect, at least down to cholesterol levels of 140-160 mg/dL (3.6-4.1 mmol/L). This association is considered causal by many individuals, consensus panels, conferences and similar groups. However, some disagree even with this causal role of elevated cholesterol and CHD risk. It seems evident from the volume of literature that the definite association of elevated cholesterol and CHD incidence is causal. Clinical trials clearly show decreased CHD mortality and nonfatal infarctions in primarily middle aged men with high total cholesterol levels after mild reductions in cholesterol over a relatively short time. Other issues such as the effect on total and non-CHD mortality and the application of these results to other population groups and lower cholesterol levels are unsettled and very much debated. Concern exists that the primary prevention trials have not demonstrated a reduction in total mortality and have shown a tendency toward increased non-CHD mortality, especially cancer and nonillness mortality. Also, most trials involve middle aged men with cholesterol levels of about 250 mg/dL (6.5 mmol/L) or greater. This paper will address pro and con considerations of these issues from the literature, followed by briefer comments on smoking and exercise and summary comments.

Discussion of the lipid hypothesis and primary prevention of CHD will be drawn from reviews and meta-analyses of the literature(14-20). These sources reference and discuss the predominant primary and secondary prevention trials and regression trials. Primary prevention trials which are discussed include MRFIT, WHO study, Oslo Study, LRC-CPPT, Helsinki Heart Study, Minnesota Coronary Survey and the Los Angeles Veterans Administration Study. Secondary prevention trials include Coronary Drug Project, MRC, Scottish Society of Physicians, Newcastle Study and Stockholm Secondary Prevention Study. Studies have demonstrated clearly independent associations of elevated low density lipoprotein (LDL) cholesterol and decreased high density lipoprotein (HDL) cholesterol with increased risk of CHD. Promising research efforts continue to find better markers for CHD risk stratification such as apolipoprotein types, LDL and HDL subtypes and Lp(a). Measurements of these and other such markers are not readily available to all practitioners and will not be addressed.

#### Points Favoring Broad Application of Primary Prevention:

a. Trials have shown significant decreases in CHD mortality and nonfatal infarctions. Some have also shown decreases in other indices of CHD morbidity such as incidence of unstable and stable angina, referral for surgery or other interventional therapy, and exercise test performance. These "quality of life" benefits must also be considered when discussing the efficacy and cost-effectiveness of cholesterol reduction programs for the primary prevention of CHD.

b. These trials were designed to test for CHD but not for total mortality; they would require much larger numbers to show an effect on total mortality. Current trials have shown results with only modest cholesterol reductions over a short follow-up. Longer follow-up and greater reduction of cholesterol level would show better results, possibly including reduction of total mortality in even these relatively small numbers of subjects.

c. Degree of risk reduction is related to the level and duration of cholesterol reduction. A 1% reduction in cholesterol equates to a 2-3% CHD risk reduction overall. However, the greatest risk reductions occur in the segments of the treatment cohorts that complied with therapy and had the most significant response to cholesterol lowering. The control groups often are treated with diet and are more closely followed than the general patient population. They might also more likely pursue individual health efforts such as smoking cessation and exercise. This would offset some of the comparative benefit in the treatment group versus the controls.

d. The increase in non-CHD mortality is not significant statistically, but only a trend which would not be present with larger studies. The apparent increased mortality is not due to a single cause and is not related to the level and duration of cholesterol reduction. This observation is therefore likely due to chance. Population studies of naturally low cholesterol individuals do not show an increase in nonillness death. There has been no significant difference in cancer incidence in most trials.

e. CHD mortality has reduced significantly in the past two decades, partly due to improved therapy but also due significantly to reduction of risk factors in the general population.

f. The success of secondary prevention trials to reduce CHD and total mortality and reduce other CHD events supports the primary prevention role of cholesterol lowering. For example, fifteen year follow-up of the niacin treatment arm of the Coronary Drug Project (21) showed decreased mortality from all causes several years after discontinuation of treatment. Successful regression of disease documented by angiography after cholesterol lowering therapy also supports this position. Regression trials will be discussed briefly later in this paper. Benefit from cholesterol lowering does not appear in these studies until 2-2.5 years after therapy is started.

#### Points Against Broad Application of Primary Prevention:

a. To be of clear benefit, primary prevention trials must show a reduction of total mortality. Neither individual trials nor meta-analyses are able to do so.

b. The occurrence of increased non-CHD deaths, especially nonillness deaths, is concerning. It is unacceptable to ascribe this to chance just because no

single specific cause is identified and because it does not make sense as a cause-effect association. Rather than eliminating this as a concern, longer follow-up trials with more patients might demonstrate more clearly that this is a real consequence of cholesterol lowering efforts. Active lowering of cholesterol levels versus naturally low cholesterol levels may not be identical biologically or physiologically and may affect endpoints very differently. The National Heart, Lung and Blood Institute Conference on Low Cholesterol(14) concluded that there is a relation between increased non-CHD deaths and both low cholesterol less than 160 mg/dL (4.1 mmol/L) and cholesterol lowering strategies. This was present in primary prevention trials but not in secondary prevention trials.

c. Current trials demonstrate reduction in CHD mortality and morbidity, but only in high risk patients. Similar results cannot be expected when the existing studies are extrapolated to other risk groups such as women, younger men, older men and individuals with lower baseline cholesterol. Many of these would be considered a lower baseline risk than the studied populations and results of intervention should be less significant.

d. Data from secondary prevention trials cannot be used to support primary prevention efforts - subjects in secondary trials have a 100% prevalence of the disease under consideration. The niacin treatment arm of the Coronary Drug Project (21) had decreased total and CHD mortality on long term follow-up after cessation of treatment but this was a secondary prevention trial in myocardial infarction survivors. Long term post-trial follow-up of the LRC-CPPT(22) showed no significant difference in total or CHD mortality; this was a primary prevention trial.

e. Current trials emphasize decreases in endpoints as a percentage decrease (relative result) rather than emphasizing absolute results. For example, a meta-analysis by Yusuf (16) reports an overall 23% risk reduction for CHD events but this is a reduction from 10.7% to 8.4%, an absolute difference of 2.3%. This represents a strikingly different impact than a 23% absolute difference in endpoint incidence between groups. This method of expressing results is accurate but it emphasizes the small segment of the population that benefits from the therapy rather than the much larger segment of the treated population that does not benefit.

f. Ravnskov (20) raised the possibility of citation bias in the literature regarding the hypothesis that cholesterol lowering prevents CHD. He reported that supportive studies are cited six times more frequently than unresponsive studies although comparable numbers of each type exist. Similar bias exist in the papers selected for meta-analyses. His meta-analysis revealed no difference in total or CHD mortality, but a decrease in nonfatal CHD events that was unrelated to duration of therapy or degree of cholesterol lowering achieved. His review included studies using estrogen and thyroxine preparations, however.

## 5. CHD REGRESSION STUDIES:

Secondary prevention trials will not be discussed. They do demonstrate much better results in reducing total mortality as well as CHD mortality and nonfatal CHD events compared to primary prevention trials. However, this would be expected because all secondary prevention trial participants have CHD and as a group are at a much higher risk of fatal CHD events. Most subjects in secondary prevention trials are survivors of myocardial infarction. It would, however, be reasonable to consider regression trials. These subjects also all have CHD, but not all have suffered a myocardial infarction. Also, the aim of primary prevention efforts in middle aged and older patients would be prevention of development of CHD and also regression of existing asymptomatic CHD. A number of studies report reduced progression and regression of coronary atherosclerotic lesions by angiography after cholesterol lowering interventions (23-28).

By serial coronary angiography in the treatment groups compared to controls, these studies demonstrate decreased progression and actual regression of baseline coronary lesions as well as decreased appearance of new lesions. More aggressive lowering of total and LDL cholesterol and more effective elevating of HDL cholesterol is achieved in these studies compared to primary prevention trials. Some studies adjust treatment levels or dosages to achieve target lipid values rather than using fixed dosages, partly explaining their greater success in improving lipid profiles. And some of these studies have accepted patients with CHD regardless of lipid values. Benefit has been seen in patients with relatively low levels of LDL cholesterol (160 mg/dL, 4.1 mmol/L). Benefit is also evident in patients with high cholesterol that respond to therapy but still remain high. Often the improvement in the lesions is only a small difference in the measured percentage of diameter reduction. However, the sophisticated quantitative measurement techniques in some of these studies allow these small changes to reach statistical significance. More importantly, CHD events are also improved in these patients. Improvement in factors other than the anatomic lesion may well play a role in their clinical improvement. These changes and improvements are seen after only a few years of therapy and follow-up. Results of long term follow-up will be very interesting when available. Regression of CHD appears to be real and achievable. The results of primary prevention trials would seem to support the concept of decreased progression and actual regression of coronary artery atherosclerosis. As has been discussed, these trials show decreased CHD mortality and nonfatal CHD events in middle aged and older men with elevated total cholesterol levels in only a few years of follow-up. It is unlikely that these results are due only to prevention of disease development in a population of this age. In many of the subjects it must be due to regression or slowed progression of existent but asymptomatic and undetected disease.

## 6. SMOKING CESSATION:

Case control and cohort studies have shown that smoking at least doubles the risk of CHD events and increases the risk of CHD mortality 70%. Risk of sudden death is significantly increased in both men and women smokers. Rate of CHD events was halved in those who stopped smoking, both for initial and recurrent CHD events. In current smokers, clear dose-response relations exist between number of cigarettes smoked per day and increasing CHD risk. In 2-5 years after smoking cessation the declining CHD risk in former smokers plateaus at a level similar to that in nonsmokers (15,29-31). In the MONICA Project (1,2) of 12 European countries following mortality and risk factor rates, some countries with high smoking rates have only mid range comparative total and CHD mortality rates. This does not negate the increased CHD risk associated with smoking. Rather it underscores the fact that many other factors are involved in CHD risk. Some are protective and serve to offset the effects of risk factors. Two recent angiographic studies (32,33) showed no association between smoking and progression/regression of coronary lesions present at baseline coronary angiography. However, smoking did correlate with development of more new lesions at follow-up angiography 3-4 years later in a dose response relation with the number of cigarettes smoked.

## 7. EXERCISE:

Although most randomized clinical trials of exercise involve subjects with known CHD, the available trials and epidemiologic studies support the concept that regular exercise reduces the risk of CHD mortality and events in both primary and secondary prevention (15-16,34-35). In Manson's review (15), a meta-analysis of exercise and CHD showed significant benefit in all groups of patients. Relative risk of CHD death was 1.9 in sedentary subjects compared with active subjects - this effect was present after adjustment for other risk factors. Overall risk reduction for CHD is as much as 50%. Blair (34) reported decreased total mortality in men and women with increasing levels of activity and decreased cardiovascular mortality in men. Decrease in mortality was most notable between the least fit and next-to-least fit quintiles, levels of fitness readily obtained. The Harvard alumni study (35) also showed significantly decreased incidence of CHD with increasing levels of activity and fitness. This protective effect was noted even in subjects who only walked regularly. College athletes who became sedentary acquired the same risk as sedentary subjects, while those who only became active later had the same lower CHD risk as college athletes who continued regular exercise.

## 8. CONCLUSION

Before addressing the question of cost-effectiveness of a therapy, one must first decide if the therapy is effective. Modifiable risk factors in our military aviators that are of interest to a CHD primary prevention program include smoking, regular exercise

and hypercholesterolemia. Routine flight medical examinations already screen for hypertension and diabetes and regulations exist for the treatment and aeromedical disposition of these two disorders apart from their contribution to CHD risk. The literature seems clear that cessation of smoking and maintenance of a regular exercise program reduce CHD risk significantly. Promotion of these two health measures can be accomplished to some degree through resources already available to the aerospace medicine specialist that serves the military aviator. The most pressing question is how to approach the cholesterol problem.

In his review of six primary prevention trials, Muldoon (19) emphasized that the trials reduced CHD mortality but did not change total mortality and increased nonillness mortality. Treatment to lower cholesterol saved 70 lives per year per 100,000 patients treated but was associated with an additional 1088 of 50 lives per year per 100,000 patients treated due to non-illness deaths. Because of these results and concerns regarding extrapolation of the benefits of cholesterol lowering to other populations, a cautious approach to population based interventions was recommended. Best results were seen in subjects with highest cholesterol levels. It was concluded that high risk groups should be targeted - significantly elevated cholesterol levels, known CHD, and multiple risk factors including cholesterol. A number of authors have constructed models to address this problem and have estimated long term benefits from cholesterol lowering therapy.

Taylor (36) applied such a model to diet therapy of asymptomatic males and females with cholesterol levels ranging from 180-300 mg/dL (4.7-7.8 mmol/L). Risk status was defined by blood pressure, smoking status and HDL cholesterol level. Age categories were 20, 40 and 60 years old. Estimated life expectancy increase in low risk groups ranged from 3 days to 3 months. In high risk groups it ranged from 2-11 months for a 6.7% decrease in cholesterol and from 5-29 months for a 20% decrease in cholesterol. Application of the model to smoking cessation and hypertension control yielded life expectancy increases of 23-70 months and 19-34 months, respectively. There was as much as an eight-fold difference in life expectancy gains if other risk factors were present and controlled. This paper underscores the debate regarding the long term benefits of cholesterol lowering. More importantly, it emphasizes the multiplicative interaction of CHD risk factors and the need for a multifactor approach to primary prevention and future research.

Grover (37) reported results of a similar model in males and females aged 35-65 years old with cholesterol levels 200-300 mg/dL (5.2-7.8 mmol/L) with and without other risk factors present. With diet and drug therapy, cholesterol reductions of 5-33% were used. Life expectancy increases ranged from .03-3.16 years and delay of onset of CHD symptoms ranged from .06 to 4.98 years. The most significant benefit was in high risk subjects. The wide variation of benefit underscores the need for better means to

identify those relatively few patients who will gain the most from intervention efforts.

Goldman (38) reported the results of a conference sponsored by the National Heart, Lung and Blood Institute. In this report, cost-effective methodology was felt to support population-wide education programs to favorably modify lifestyles and to support medical therapy for secondary prevention. Medical therapy for primary prevention was cost-effective only in high risk individuals and the cost of specific medications must be considered. Primary prevention became more favorable as other risk factors were added. The cost in 1990 dollars of community-wide education programs was estimated at approximately \$13.50 per person per year.

In addition to screening for and treating hypertension and diabetes, the aerospace medicine community should promote to the entire military aviation population lifestyle changes of smoking cessation, regular exercise programs, and a diet designed to improve the lipid profile. If the incidence of CHD can be reduced in lower risk population groups, it can best be done (possibly only be done) by such a population-based approach. Screening for lipid profile and other risk factors should be done to identify high risk aviators for more intensive diet therapy and/or drug therapy for improvement of the lipid profile and to improve other risk factors. What lipid profile values should define the need for individual and more aggressive intervention? Several panels and consensus groups have addressed this issue. The most familiar include the National Cholesterol Education Program (NCEP)(39), the Toronto Working Group (40), the Canadian Consensus Conference( 41), the European Atherosclerosis Society (42) and the British Cardiac Society Working Group (43). The NCEP guidelines have been widely criticized, primarily for being too aggressive. Based on a review of the literature, the Toronto Working Group policy seems to be more in accord with all the pro and con issues of this problem. It targets high risk individuals that most clearly benefit from aggressive diet and drug CHD preventive measures. The evidence from the literature is sufficient - the aerospace medicine community should adopt some policy of primary prevention of CHD and pursue it enthusiastically in the military aviation population. Details of the policy may need to vary between countries due to such factors as overall characteristics of the aviator population and available resources.

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## AEROMEDICAL DISPOSITION OF ARRHYTHMIAS AND ELECTROCARDIOGRAPHIC FINDINGS IN AIRCREW

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### SUMMARY:

Screening asymptomatic individuals for occult cardiac disease continues to be a difficult task. One of the standard screening procedures continues to be electrocardiography. Electrocardiography is neither a sensitive nor specific tool in identifying heart disease but continues to offer useful information. Interpretation of these studies for aeromedical purposes requires an appreciation for certain differences between a standard clinical population from which the significance of most ECG findings were obtained and the asymptomatic generally healthy aviator population. The United States Air Force Central Electrocardiographic Library is the repository for all electrocardiograms obtained on Air Force aviators. This facility was established in 1957 in order to review electrocardiograms performed on Air Force aviators to determine the significance of electrocardiographic findings in asymptomatic individuals and to provide consultative services to local flight surgeons as well as the Surgeon General. The following sections discuss the major classes of electrocardiographic findings, their significance and additional evaluations required by the USAF.

### SINUS BRADYCARDIA:

The standard definition for sinus bradycardia is a sinus rate less than 60 beats per min. Sinus bradycardia also requires a normal P wave axis and a PR interval of at least 0.12 sec. Since most aviators are young and well conditioned, sinus bradycardia is a common finding. In one study (1) performed at the USAF School of Aerospace Medicine (USAFSAM), sinus bradycardia was present in 25% of individuals under the age of 20. This percentage decreased to approximately 19% of individuals by the age of 35. This is probably associated with normal loss of vagal tone with advancing age. Because of its frequency in our population, sinus bradycardia has been defined for aeromedical reasons as a heart rate of less than 50 beats/min. In our population, sinus bradycardia to 40 beats/min. is considered a normal variant and no further evaluation is required. Slower rates however, may be associated with the presence of sinus node dysfunction. In aviators with heart rates of less than 40 beats/min., a rhythm strip is performed during exercise such as calisthenics. Moderate exercise should produce an appropriate increase in heart rate. A heart rate increase to at least 100 beats/min. is generally expected. If this cannot be achieved, a treadmill test and Holter monitor are requested in order to better document the heart rate response to exercise as well as to screen for marked sinus

bradycardia, sinus pauses, or tachyarrhythmias that may be associated with sick sinus syndrome. If these tests are normal, no further evaluation is requested. If these tests still suggest the possibility of sick sinus syndrome, electrophysiologic testing should be performed. Aviators with sinus bradycardia and a normal heart rate response to exercise and no evidence of sinus node dysfunction are qualified for all flying duties as well as entry into flying training. Aviators with sinus node dysfunction are disqualified from all flying duties.

### SINUS TACHYCARDIA:

Sinus tachycardia is defined as a sinus rhythm with a heart rate greater than 100 beats/min. Sinus tachycardia is generally up to 150 to 160 beats/min. but in a young healthy aviator population it may occasionally exceed 200 beats/min. with strenuous exercise. In a review of ECGs from the ECG Library (1) sinus tachycardia occurred on 4.2% of resting electrocardiograms on individuals age 16 to 19. This decreased with increasing age to 2.09% in a 30 to 34 year age group. The primary cause for tachycardia on a resting electrocardiogram is probably anxiety. Sinus tachycardia may also be caused by recent use of tobacco products, alcohol, caffeine beverages or over the counter cold preparations. Since a sinus tachycardia is a relatively uncommon finding in a healthy pilot population, a repeat resting electrocardiogram should be performed after insuring that the subject is comfortable and in the resting state. If a persistent sinus tachycardia exists, further evaluation should be performed to exclude a hyperadrenergic state, hyperthyroidism, or other underlying causes. A sinus tachycardia may be a normal variant if there are no secondary causes identified and is not disqualifying for continued flying duties or training.

### SUPRAVENTRICULAR RHYTHM ABNORMALITIES:

#### Sinus Pause

A sinus pause or sinus arrest results from failure in pulse generation at the sinoatrial node. On a resting electrocardiogram or rhythm strip, a sinus arrest appears as a long pause during sinus rhythm with no P wave. A sinus pause may be seen in a healthy individual because of increased vagal tone. In the aviator population, this may occasionally be the result of sick sinus syndrome. Sinus pauses should be differentiated from blocked premature atrial contractions, sinoatrial block, or a sinus arrhythmia.

Sinus pauses on a resting electrocardiogram are generally evaluated with a Holter monitor paying close attention to symptoms during episodes of recurrent sinus pauses. Asymptomatic sinus pauses of 3 to 4 seconds may occur in otherwise healthy individuals. The timing of sinus pauses should be considered when the Holter monitor is reviewed since these are more common at times of rest or during sleep but would be more inappropriate during times of physical activity. A treadmill test may also be helpful in determining the individual's heart rate response to exercise. If sinus pauses still seem to be inappropriate after reviewing the Holter monitor and treadmill test, an electrophysiologic study may be necessary to further evaluate sinus node function.

#### Supraventricular Premature Contractions

Premature atrial contractions (PACs) occurred in our population in 0.043% of resting ECGs (1). Premature nodal contractions (PNCs) were also noted in 0.021% of ECGs (1). Most aviators with supraventricular premature contractions (SVPCs) have no underlying heart disease. In one study (2) 283 middle aged men underwent Holter monitoring for 6 hours. SVPCs were identified in 76% of subjects. SVPCs may also occur as a result of organic heart disease primarily involving the atrium. Individuals with mitral stenosis or cor pulmonale with atrial enlargement have frequent PACs as well as supraventricular tachycardias (SVT) including atrial fibrillation and atrial flutter. In an individual found to have SVPCs on a resting electrocardiogram, a careful history and physical exam should be performed. This history should include questions related to possible symptoms from premature complexes or runs of SVT. Questions should also be directed at precipitating causes such as ingestion of stimulants like tobacco products, caffeine, or alcohol. Ingestion of medications such as over the counter cold preparations may also precipitate SVPCs. A physical exam should pay particular attention to findings suggesting mitral stenosis or significant mitral regurgitation. A 24-hour Holter monitor should also be obtained to better quantify the frequency of SV ectopy. If the SV ectopy consists of only isolated or paired SVPCs and if the history, physical, and ECG does not suggest a likely cause, no further evaluation is needed. If there is a concern for underlying heart disease, an echocardiogram would be useful to evaluate valvular function and atrial abnormalities. Thyroid function studies may also be helpful if the history suggests hyperthyroidism.

#### Supraventricular Tachycardia (SVT)

SVT is defined as three or more supraventricular ectopic beats in a row at a rate of 100 beats/min. or greater. SVT generally refers to atrial tachycardia, junctional tachycardia, atrial fibrillation, atrial flutter and multifocal atrial tachycardia. All types of SVT were disqualifying in the U.S. Air Force (USAF) until the beginning of the SVT Study Group in 1973. At that time, there was evidence that individuals with rare episodes of SVT without underlying heart disease enjoyed a favorable prognosis and could be returned

safely to flying duties. Individuals with recurrent SVT or individuals with SVT associated with heart disease were felt to represent an increased risk and were still disqualified from flying duties. Our experience with 430 aviators with SVT excluding multifocal atrial tachycardia (MAT), atrial fibrillation, and atrial flutter was evaluated by reviewing their Aeromedical Consultation Service (ACS) medical documents and by telephone and written survey. Follow-up was obtained on 99% of these individuals and the data was reviewed to examine the cofactors that predicted an unfavorable outcome. The mean follow-up for this group using ACS evaluations and questionnaires was 11.4 years. Most of these aviators had a single brief run of SVT but 20% had runs lasting more than 10 min. Most runs occurred in the range of 150 beats/min. but 16% had rates exceeding 220 beats/min. Most episodes of SVT occurred at rest although 18% occurred during exercise with an additional 10% occurring during both exercise and at rest. Although 25 individuals died during the study, there were no deaths caused by or related to the SVT. There were, however, five individuals with syncope, 20 with presyncope or light-headedness, 11 with chest discomfort and dyspnea felt secondary to SVT, and 6 with episodes of tunnel vision. There were also 21 individuals with asymptomatic, recurrent, sustained ( $\geq 10$  min.) SVT. In all, 42 (10%) had symptoms of hemodynamic compromise and 21 (5%) had recurrent sustained SVT. Multiple factors were examined in an attempt to identify indicators for individuals that would develop hemodynamic compromise or recurrent sustained episodes of SVT. These factors included the presence of cardiac conditions such as mitral valve prolapse, Wolff-Parkinson-White (WPW) syndrome, coronary artery disease, or bundle branch blocks. Other factors such as heart rate during SVT, length of the initial SVT, and symptoms at presentation were also examined. The only cardiac condition over represented in those with hemodynamic compromise or recurrent sustained episodes was WPW syndrome. In addition, 90% of individuals with symptomatic SVT initially presented with these symptoms. The remaining 10% that later went on to develop symptoms, initially presented with either sustained or recurrent sustained SVT. This study documented that most individuals with asymptomatic SVT remained healthy and symptom free for many years. Even individuals with a single prolonged episode of SVT had a good prognosis. Only those individuals with WPW pattern on ECG with SVT or recurrent sustained SVT were at high risk for future symptomatic events. Those individuals with mitral valve prolapse and SVT had a prognosis similar to aviators with SVT alone. As a result of the SVT Study Group, significant changes have been implemented in the required medical evaluation and subsequent waiver recommendations for these individuals. Aviators with a single, asymptomatic, brief run of SVT (3 to 10 beats duration) require a local evaluation including an internal medicine consultation, thyroid function test, three Holter monitors performed over 3 months, an echocardiogram, and treadmill test. If these studies are unremarkable and show no recurrent SVT, no further evaluation is requested and the aviator

is returned to unlimited flying duties. Aviators with longer or recurrent episodes of SVT require an evaluation at the ACS. Flying Class II unrestricted waivers are recommended for aviators with single or recurrent non-sustained SVT or a single episode of sustained SVT. This is also true when this degree of SVT is seen in association with mitral valve prolapse, sarcoidosis, left or right bundle branch block or valvular heart disease other than aortic insufficiency. A non-high performance waiver is recommended for individuals with rare recurrent sustained SVT (3 years or more between episodes). A non-high performance waiver is likewise recommended for single or recurrent non-sustained SVT and the presence of minimal coronary disease, ventricular tachycardia or aortic insufficiency. A non-high performance waiver is also recommended for a single sustained episode of SVT with ventricular tachycardia and aortic insufficiency. The restriction to non-high performance flying in individuals with SVT in the previously listed cardiac abnormalities is appropriate since the conditions of minimal coronary artery disease, ventricular tachycardia and aortic insufficiency already require a non-high performance waiver for the USAF. Permanent disqualification from flying duties is recommended for any individual with hemodynamically unstable SVT, recurrent sustained SVT when the interval between episodes is 3 years or less, any SVT associated with pre-excitation syndrome or a single sustained episode of SVT associated with gradable coronary artery disease.

#### VENTRICULAR RHYTHM ABNORMALITIES:

##### **Premature Ventricular Contractions**

Premature ventricular contractions (PVCs) are very common in healthy individuals as well as patients with significant heart disease. In our population, PVCs occurred in 0.78% of resting electrocardiograms (1). PVCs were found very infrequently in the younger age groups but increased steadily in frequency with increasing age. The likelihood of identifying PVCs is dependent upon the length of observation. Hinkle et al (2) studied 283 actively employed American men using a 6-hour ambulatory electrocardiographic recording. PVCs were identified in 62% of these individuals. Although PVCs are commonly seen in normal individuals, ventricular ectopy is also seen in association with coronary artery disease, cardiomyopathies, hypertension and abnormal metabolic states. PVCs on a resting electrocardiogram should prompt a careful history and physical examination and a 24-hour Holter monitor recording. Rare or occasional ( $\leq 1\%$ ) PVCs are a normal finding and further evaluation or restriction from flying duties is not recommended. Individuals with frequent ( $>1\%$ ) ventricular ectopy or ventricular couplets should be further evaluated with an echocardiogram and treadmill exercise tolerance test. If these studies are normal, no further evaluation is recommended. If a Holter monitor shows very frequent ( $>10\%$ ) PVCs, a complete cardiac evaluation at the ACS should be performed.

##### **Ventricular Tachycardia**

Ventricular Tachycardia (VT) is defined as three ventricular premature complexes in a row at a rate exceeding 100 beats/min. VT may also occur in asymptomatic healthy individuals but is also associated with coronary artery disease, cardiomyopathies, significant valvular disease, and infiltrative processes. Aviators with ventricular tachycardia should undergo an internal medicine evaluation to insure that they are medically stable. This includes a thorough history and physical in an attempt to identify symptoms and to uncover precipitating causes. If they are stable, then they should undergo a treadmill exercise tolerance test and echocardiogram. If significant underlying heart disease is identified, they should be treated clinically as necessary. If these studies are unremarkable, they should also undergo three Holter monitors over the next 3 months to better define the frequency and recurrence rate of VT. Recurrent VT is disqualifying and routine clinical follow-up is recommended. If the aviator has no recurrent VT and there is no evidence of underlying heart disease, he should be referred to ACS for further evaluation. This further evaluation includes complete non-invasive studies and cardiac catheterization if the individual is 36 years of age or older, or younger than 36 if he has significant risk factors for coronary artery disease. Individuals with a single brief asymptomatic run of VT with no underlying heart disease are returned to non-high performance flying duties. Individuals with recurrent VT or heart disease are disqualified and treated clinically.

The medical literature generally stratifies the risk of individuals found to have VT based on the presence or absence of underlying heart disease. The outcome of patients with VT and significant coronary disease, prior myocardial infarctions or cardiomyopathies is described well enough in the literature to dispense with further consideration for continued flying duties in this population. Although there are case reports of sudden death occurring in patients with VT and no heart disease, the medical literature generally describes idiopathic VT as having a benign prognosis. Unfortunately, this is based on a clinical viewpoint and further consideration should be made before applying this view to an occupational arena.

A commonly quoted study on this topic was published by Kennedy et al (3). They stated, "We conclude that the long-term prognosis in asymptomatic healthy subjects with frequent and complex ventricular ectopy is similar to that of healthy US population and suggests no increase risk of death". Similar reports in the medical literature form the basis for the clinical decisions made regarding appropriate medical evaluation and subsequent therapy for patients with VT. Closer examination of Kennedy's article is warranted before applying their conclusions to the realm of aerospace medicine.

This study followed 73 asymptomatic healthy subjects who were found to have frequent and complex



ventricular ectopy on a 24-hour Holter monitor. The mean frequency was 566 ventricular ectopic beats/hr. with multifocal ventricular ectopy in 63%, ventricular pairs in 60%, and ventricular tachycardia in only 26%. Asymptomatic healthy status was confirmed by "extensive non-invasive cardiac examination, although cardiac catheterization of a subsample of subjects disclosed serious coronary disease in 19%". Follow-up for 3 to 9.5 years (mean follow-up of 6.5 years) was accomplished in 70 subjects (96%). The mean age upon entry into the study was 46.0 plus or minus 13.3 years. Eighty percent were men and the majority were white. "Follow-up data for 70 subjects who were asymptomatic initially showed that 21% had experienced bothersome palpitations and 15% reported some form of chest discomfort or angina pectoris. Cardiovascular events were detected in five subjects. One subject has an episode of syncope and the results of a subsequent cardiac catheterization, coronary angiography and electrophysiologic study were all normal." "Instantaneous sudden death occurred in one male subject (41 years of age) who had previously been documented to have normal coronary angiograms and catheterization data after 7.3 years of follow-up."

The conclusion that complex ventricular ectopy is benign in spite of these complications and symptoms is based on a comparison with a standard mortality ratio calculated with the use of Morton's US white and non-white death rate data (8th revision) for 448 person years of follow-up (4). This calculation predicted 7.4 deaths whereas only 2 deaths occurred in the 70 subjects followed. Although three subjects were lost to follow-up, the author states that assuming that deaths occurred in those three, the conclusion remains unchanged. In order to accept the conclusion of this paper, you must also accept 7.4 deaths out of a group of 73 pilots. This is based on using life tables statistics for the general population to predict the outcome. This seems unreasonably high for a pilot population.

There are several other obvious limitations to this study. There is an absence of concurrent controls and there was a small sample size. In addition, at the time of the study follow-up, 27% of the subjects were receiving Beta blocker drug therapy. Beta blockers have proven to be very effective drug for ventricular ectopy and are one of the few drugs that have been shown to improve survival in certain patients with coronary artery disease. This paper has been found in clinical circles to be adequate to base decisions regarding further evaluation and therapy. In fact, this is the article referenced by the American Heart Association and the American College of Cardiology Task Force (5), "Report on Guidelines for Ambulatory Electrocardiography". This task force report references this paper when it states that "premature ventricular complexes and even VT if detected by ambulatory electrocardiography in asymptomatic patients without organic heart disease have virtually no predictive value for future cardiac events". Although the study has been adequate for clinical purposes, we do not believe that it provides a sufficiently reassuring

prognosis for aeromedical purposes. Of the 70 asymptomatic subjects followed, 21% had bothersome palpitations, one subject experienced syncope with a normal cardiac catheterization, and one subject experienced instantaneous sudden death with a previously normal cardiac catheterization. Although this outcome may be expected in a hospital based population, this complication rate seems inappropriate for a pilot population. The article clearly underscores the difference in the meaning of a "good prognosis" when describing populations based on clinical cardiology versus a flying squadron. The acceptable probability of mortality and morbidity in a clinic-based population are clearly different than the "acceptable" probability for mortality and morbidity for aviators.

A second paper by Tanabe et al (6) looked at non-death end-points for VT. The author studied 117 patients with VT with ischemic heart disease, idiopathic cardiomyopathy, miscellaneous heart disease and idiopathic VT. The mean follow-up was 46.8 months plus or minus 32.0 months. Thirty three patients had idiopathic VT without evidence of organic heart disease. There were no sudden deaths in this group, but six subjects had syncope. Patients with syncope had a significantly higher VT rate than those without syncope. Their conclusion was "it is suggested that idiopathic VT is not related to cardiac sudden death but careful attention should be paid to syncope when a rapid VT rate is observed...".

A third article by Goy et al (7) also underscores a significant occupational concern for idiopathic ventricular tachycardia. The author states "we conclude that patients with VT and no detectable heart disease have good long-term prognosis and that appropriate therapy can be found in almost all patients". A close review of this article places this statement in prospective. The author studied 20 patients with VT and "no detectable heart disease". Of interest, three patients (15%) had a mid-systolic click suggesting mitral valve prolapse (MVP) and had MVP on echocardiogram without either regurgitation or redundant valve. The mean age was 44 years old. Symptoms were present in 18 patients. Eight had syncope, ten had palpitations or dizziness. VT was sustained in 11 patients. Medical therapy was started in 19 patients. During the mean follow-up of 10 years, one patient died suddenly. He had stopped taking Amiodarone 5 months before. In seven patients, symptoms recurred and were due to discontinuation of therapy in two cases and inefficacy of previous treatment in five patients. After modification of treatment (three cases), implantation of a pacemaker (one case), and catheter ablation (one case), all patients became asymptomatic.

These articles all purport to show a benign prognosis for individuals with idiopathic ventricular tachycardia. From a clinical standpoint, these are acceptable statements but should be taken in the context of a clinical population. Because of the actual outcome of these patients, we continue to remain concerned about patients with idiopathic VT.

### FIRST DEGREE AV BLOCK:

A first degree atrial ventricular block (AVB) is defined as a PR interval greater than 0.20 sec. This interval may be fixed but is frequently seen to fluctuate in normal individuals. This interval may normally shorten with elevated heart rate and is more prolonged in certain periods of high vagal tone. Hiss and Lamb (1) found an incidence of first degree AVB on resting electrocardiograms of 0.7%. Because of the low resting heart rate and high vagal tone of most aviators, first degree AVB has been defined aeromedically as PR interval of greater than or equal to 0.22 sec. Although this is generally a normal finding, first degree AVB may also be associated with advancing age (without evidence of other heart disease), myocarditis, myocardial infarction, sick sinus syndrome, acute rheumatic fever, or medications including digitalis, quinidine, procainamide, or metabolic conditions such as hyperkalemia or uremia.

Individuals with first degree AVB based on increased vagal tone will decrease their PR interval with exercise at increased heart rates. An ECG recording should be obtained during calisthenics such as running in place or other maneuvers. If the PR interval shortens and becomes normal with increased heart rate, the first degree AVB is considered a normal variant. If this PR interval shortening is not easily demonstrated on a rhythm strip, a standard treadmill test or Holter monitor may be necessary. If the PR interval is not normalized with exercise, a full cardiac evaluation should be performed in order to rule out the possibility of significant underlying conduction system disease.

### SECOND DEGREE AV BLOCK:

#### **Mobitz Type I**

A Mobitz Type I second degree AVB is intermittent failure of an atrial impulse to be conducted to the ventricles. P waves occur with an increasing PR interval until a blocked P wave occurs. Atrioventricular conduction then returns and another cycle is generally repeated. The conduction ratio can be 2:1, but is frequently 3:1, 4:1, or more. In addition to lengthening PR interval, there is also a shortening of the R to R interval until a P wave is blocked. A Mobitz Type I second degree AVB is commonly found in healthy well conditioned individuals as a normal variant. It is frequently seen in a state of high vagal tone. In our population, this is considered a normal variant and no further evaluation or flying restriction is recommended.

#### **Mobitz Type II**

In a Mobitz Type II second degree AVB there is intermittently blocked P waves but the PR interval remains constant in the conducted beats. In most cases, the block is distal to the bundle of His, but may occasionally be within the bundle of His itself. This is frequently associated with a bundle branch block

(BBB). The type II second degree AVB is often a precursor of third degree AVB and an indication of significant conduction system disease. A permanent pacemaker is often indicated. Because of the significant risk of incapacitating symptoms, this block is disqualifying for all flying duties.

### THIRD DEGREE AV BLOCK:

In third degree AV block antegrade conduction between the atria and ventricles is completely interrupted and the atria and ventricle are activated independently. The atrial rate is faster than the ventricular rate. The ventricular rhythm is maintained by either a junctional or an idioventricular pacemaker. This may occur as a congenital finding in the absence of other underlying heart disease but when diagnosed in an adult it is usually associated with heart disease. Since synchrony of atrial and ventricular contraction is lost, the individual has decreased cardiac output and a decreased heart rate response to activity resulting in decreased exercise tolerance and a predilection for symptoms of syncope and presyncope. Possible etiologies include the toxic effects of various medications such as digitalis, myocardial infarction, myocarditis, coronary artery disease, chronic degenerative changes in the conduction system, infectious processes and electrolyte imbalances. Third degree AV block generally requires a permanent pacemaker. This condition is disqualifying for flying duties.

### AXIS DEVIATION:

#### **Right Axis Deviation**

Electrocardiographic criteria for right and left axis deviation varies between sources. Right axis deviation (RAD) has been described as an axis in the frontal plane greater than 90°, 100°, or 120°. At the ACS, RAD is defined as a mean QRS axis of 120° or more in the frontal plane. Hiss and Lamb (1) found RAD in 0.1% of initial electrocardiograms. The incidence was highest in young individuals aged 18 to 29. Isolated RAD in a young asymptomatic individual generally represents a persistent juvenile pattern and is considered a normal variant. In individuals over 45 years of age, RAD as an initial finding usually occurs only in those with known heart disease or pulmonary disease. If a RAD is a new finding in an individual over 35 years of age, an Internal Medicine evaluation is recommended to evaluate the possibility of significant pulmonary disease as well as an echocardiogram. If RAD is found as an initial finding in an individual 35 years or less no further evaluation is recommended.

#### **Left Anterior Hemiblock**

Left anterior hemiblock is defined as: (1) displacement of the mean QRS axis in the frontal plane between -45° and -90°, (2) a qR complex (or an R wave) in lead I and AVL, an rS complex in leads II, III, and AVF, and (3) normal or slightly prolonged QRS duration. In the Tecumseh study (8) of 4,678 individuals an abnormal left axis was identified in 5%. Fifty-nine

percent of individuals with left axis deviation (LAD) had other findings suggestive of heart disease. Eliot, et al (9) examined 195 asymptomatic men with marked LAD. During the initial evaluation and follow-up of 22 months, 58% were found to have cardiovascular disease or diabetes. Thirty four percent had evidence of coronary artery disease, 14% had hypertension, and 7% had subclinical diabetes mellitus. In most of the clinical pathologic series, CAD was by far the most common cause of LAD. This occurred either with or without myocardial infarction. Hypertensive heart disease, aortic valve disease and primary and secondary cardiomyopathies are also common causes of LAD. Among patients without apparent heart disease, left anterior hemiblock may be caused by degenerative disease of the conducting tissue or sclerosis of the left side of the cardiac skeleton. Among acyanotic congenital heart diseases abnormal LAD is seen most commonly in patients with endocardial cushion defects which include atrial septal defects of the primum type, atrial ventricular canal, and common atrium. In isolated ventricular septal defect, LAD occurs in about 4% of cases. In cyanotic congenital heart disease, LAD typically occurs in patients with tricuspid atresia. Isolated congenital LAD without evidence of heart disease has also been reported.

If left hemiblock is present in an aviator as a significant sudden change from prior ECGs, this should be considered a significant conduction disturbance and an ACS evaluation is recommended. If left anterior hemiblock is found in an individual 35 years of age or younger and no prior tracings are available, an echocardiogram is recommended to rule out the presence of congenital heart disease. If left anterior hemiblock is identified in an aviator over 35 years of age and no prior tracings are available, a treadmill test and echocardiogram should be performed to rule out the additional possibility of coronary artery disease as the cause. If left anterior hemiblock had been present and stable for many years, only an echocardiogram is recommended. If the findings of a left anterior hemiblock develops slowly over many years as a result of progressive leftward axis deviation and is not a new or sudden change, no further evaluation is generally recommended.

#### **Left Axis Deviation (LAD)**

Although most authors use the terms left anterior hemiblock and left axis deviation interchangeably at the ACS, LAD is defined as a mean QRS axis equal to or more negative than  $-30^\circ$ , but without full criteria for left anterior hemiblock. His and Lamb (1) found a frontal plane QRS axis between  $-30^\circ$  and  $-90^\circ$  in 1.0%. LAD as a serial change should be evaluated with a treadmill test and echocardiogram. If LAD is a new finding and prior tracings are not available, the workup is the same as for a left anterior hemiblock. If the LAD developed as a slow progressive shift and has been present for many years, no evaluation is recommended.

#### **RIGHT BUNDLE BRANCH BLOCK (RBBB):**

The diagnostic criteria for a RBBB includes: 1. A QRS interval of 0.12 sec. or greater. 2. A wide S wave in the lateral precordial leads and 3. A secondary R (R) wave in leads V1 and V2. Acquired RBBB discovered on serial electrocardiograms is present in approximately 0.6% of all aviators with a gradual increased incidence with age. Rotman and Triebwasser (10) reported on 394 patients studied at the USAFSAM with complete RBBB. Three hundred seventy-two of these individuals had complete evaluations including electrophysiologic studies. Ninety-four percent had no evidence of heart disease. Three percent had CAD. Two percent had hypertensive heart disease. One percent had other abnormalities including an abnormal His bundle study. There was greater than 10 years follow-up in 95% of the subjects. Six percent ultimately developed coronary disease or hypertension and less than one percent suffered cardiac death. Previous studies performed and reported at USAFSAM (11) showed the right bundle branch to be intact with the block located distally at the level of the Purkinje fibers beyond the moderator bend. Progressive conduction system disease was felt to be unlikely. In fact, a progressive block occurred in only 1 of 394 patients reported in a follow up of over 10 years. RBBB was also not found to be a marker for either coronary disease or cardiomyopathy. RBBB, therefore, is recommended for waiver for all classes of flying duties after an otherwise normal non-invasive evaluation at the ACS. No specific follow-up is recommended for individuals with RBBB after their initial evaluation.

#### **LEFT BUNDLE BRANCH BLOCK (LBBB):**

The diagnostic criteria for a LBBB include: 1. A QRS duration of 0.12 seconds or greater, 2. Broad monophasic R wave in the lateral precordial leads, 3. Absence of a Q wave in the lateral precordial leads, 4. Displacement of the ST segment and T wave in a direction opposite to the major deflection of the QRS complex. In reviewing ECG tracings on over 122,000 individuals, Hiss and Lamb (1) identified a LBBB in 0.013%. There were no individuals with LBBB under the age of 25 and most were found in the 35 to 39 year-old age group. Coronary artery disease and hypertension are the most common causes of LBBB. Most clinical studies suggest that approximately 70% of patients with a LBBB have evidence of ischemic heart. In addition to ischemic heart disease, LBBB is also associated with primary and secondary cardiomyopathies, rheumatic heart disease and calcific aortic stenosis. When seen in the absence of overt heart disease, this may be secondary to a primary degenerative disease of the conducting system, or may be an isolated finding with no other evidence of cardiac disease. Aviators found to have a persistent or intermittent LBBB are disqualified from flying duties and are required to undergo complete evaluation at the ACS. This evaluation includes a complete noninvasive cardiovascular evaluation as well as a left heart catheterization for left ventriculography and coronary angiography and a right heart catheterization for a limited electrophysiologic study to determine the

integrity of the remaining conduction system. Individuals with a markedly prolonged H-V interval (HIS-ventricular interval) are disqualified from flying duties because of the possibility of progressing to complete heart block. Individuals without evidence of higher degree of heart block, normal angiography, normal left ventricular function, and a normal H-V interval are returned to unrestricted flying duties. A LBBB remains disqualifying for entry into flying duties.

#### ATRIAL ABNORMALITIES:

The correlation between true atrial enlargement or hypertrophy and abnormalities seen on the routine electrocardiogram is relatively poor. The criteria for left atrial enlargement are: 1. The P terminal force in lead V1 is equal to or more negative than -0.04 mm.-sec. (This measurement is the product of the depth of the terminal negative deflection and its duration.) 2. The P wave is notched with a duration of 0.12 sec. or more. 3. A leftward shift of the P-wave axis in the frontal plane to 15° or beyond or a leftward shift of the terminal P force in the frontal plane (12). The criteria for right atrial enlargement are: 1. The P wave is tall and peaked with a height of 2.5 mm. or more in leads II, III, and AVF and has a normal duration. 2. The P wave axis in the frontal plane is 75° or greater. 3. The positive deflection of the P wave in leads V1 or V2 is greater than 1.5 mm. (12). When left or right atrial enlargement is identified on a resting electrocardiogram as an initial finding or as a serial change, an echocardiogram is required. If atrial enlargement is found, an ACS evaluation should be requested. If the echocardiogram is normal, no further evaluation is necessary for this finding.

#### LEFT VENTRICULAR HYPERTROPHY:

There are a number of ECG criteria for the diagnosis of left ventricular hypertrophy (LVH). These include voltage criteria in addition to left axis deviation, delayed intrinsicoid deflection, and secondary ST and T wave abnormalities. Although numerous diagnostic criteria are available, the USAF Electrocardiography Library (ECG) uses the following criteria: the sum of the S wave in V1 or V2 plus the R wave in V5 or V6 is greater than 55 mm. in individuals under the age of 35 and greater than 45 mm. in individuals 35 or older. Unfortunately, none of the ECG criteria are very specific for LVH. If a resting ECG exceeds our voltage criteria for LVH, an echocardiogram is requested. If the echocardiogram demonstrates normal wall thickness then the increased voltage on the resting electrocardiogram is considered normal variant. If the echocardiogram shows LVH, the aviator is disqualified and an ACS evaluation is requested. If that evaluation demonstrates hypertension or cardiac disease as the cause of left ventricular hypertrophy, permanent disqualification is recommended. If mild left ventricular hypertrophy is identified without evidence of organic heart disease or secondary cause, a thorough exercise history is obtained. A vigorous exercise program may be responsible for some mild degree of LVH. Under these circumstances, the

aviator is counseled against any strenuous exercise and a repeat echocardiogram is performed within the next several months. If this demonstrates regression, then the aviator is felt to have an athletic heart syndrome and is returned to unrestricted flying duties. If left ventricular hypertrophy is felt to be secondary to a hypertrophic cardiomyopathy, the aviator is disqualified from all flying duties and referred for routine medical follow-up.

#### RIGHT VENTRICULAR HYPERTROPHY:

There are also multiple criteria for the electrocardiographic diagnosis of right ventricular hypertrophy (RVH). Unfortunately, these criteria are also quite nonspecific. If an aviator has ECG criteria for RVH, an echocardiogram is also performed. If there is no evidence of RVH or pulmonary hypertension, the ECG findings are considered a normal variant and no further evaluation is requested. If RVH is identified, the aviator is disqualified and further medical evaluation is pursued to identify the cause of this abnormality.

#### PRE-EXCITATION SYNDROMES:

##### Wolff-Parkinson-White Syndrome

The ECG diagnosis of Wolff-Parkinson-White (WPW) electrocardiographic pattern is a short PR interval (usually less than or equal to 0.10 sec.), a delta wave, and a wide QRS complex. Individuals with WPW syndrome have both the electrocardiographic pattern as well as a tachyarrhythmia. Approximately 0.15% to 0.2% of the general population have a WPW pattern on electrocardiography. Although most individuals with WPW probably remain asymptomatic, a certain subpopulation develop significant tachyarrhythmias. The most common tachycardia is paroxysmal supraventricular tachycardia. Heart rates may range from 150 to 250 beats/min. or faster. A less common tachyarrhythmia includes atrial fibrillation and atrial flutter. Ventricular rates may be as rapid as 220 to 350 beats/min. When ventricular rates become excessive, the rhythm may degenerate into ventricular fibrillation and ultimately in death. Because of this concern, WPW pattern on resting electrocardiogram is considered disqualifying for flight training. Individuals with asymptomatic WPW pattern are thoroughly evaluated at the ACS and are returned to flying duties if they have no evidence of tachyarrhythmias. Individuals with tachyarrhythmias are disqualified from all flying duties. At this time, the ACS is undertaking a review of all asymptomatic incidentally found cases of WPW to determine the prognostic significance of this finding in our population.

A new development in the therapy for WPW syndrome includes radio frequency catheter ablation. This procedure isolates and ablates the by-pass tract responsible for pre-excitation. Although the long-term results and complications of radio frequency catheter ablation are not known, the short-term results and complication rate appear to be encouraging. At this time, the U.S. Air Force is undertaking a study to

evaluate all aviators who underwent catheter ablation for clinical reasons. These individuals are followed for six months after catheter ablation with multiple Holter monitors. If there is no evidence of a recurrence of the bypass tract, a complete ACS evaluation is performed including an electrophysiologic study to rule out the possibility of a concealed pathway. If individuals with catheter ablation show no evidence of a residual bypass tract, they will return to unrestricted flying duties. At this time, individuals with WPW pattern and nonsustained tachyarrhythmias remain disqualified for continued flying duties.

#### The Lown-Ganong-Levine Syndrome

The Lown-Ganong-Levine Syndrome (LGL) is characterized by a short PR interval and normal QRS complex without a delta wave, but with associated tachyarrhythmias. This syndrome is also disqualifying for flying training as well as classes of flying duties. In the absence of a tachyarrhythmia there are no characteristic electrocardiographic features of this syndrome other than the short PR interval. However, a short PR interval may also be a normal variant and is not diagnostic of accelerated conduction. Because of this, a diagnosis of LGL is only made in association with tachyarrhythmias. Evaluation is generally not performed in aviators demonstrating only a short PR interval and normal QRS complex.

#### Q-WAVES:

Significant Q-waves on a resting electrocardiogram suggest the presence of scarred myocardium generally from a prior myocardial infarction. Diagnostic criteria include Q-waves that are 0.04 sec. or greater in duration with a depth of one-quarter to one-third height of the R-wave. A myocardial infarction is permanently disqualifying and a waiver is not recommended for continued flying duties. The primary concern is for an incapacitating dysrhythmia or for the development of angina or a second myocardial infarction. Occasionally inferior Q-waves are seen without a prior history of myocardial infarction. A repeat ECG during inspiration and expiration may normalize the electrocardiogram. These small changes in axis eliminate the Q-waves and this is considered a normal variant and no further evaluation is requested. If the local evaluation does not resolve this question and the aviator is stable and asymptomatic, an ACS evaluation is requested. During this evaluation, a treadmill test, thallium scan and echocardiogram are performed. Although a treadmill test may be normal post-infarction, it may also demonstrate other areas of ischemia in the remaining myocardial. The results of the treadmill test may also help stratify individuals into varying degrees of risk. The thallium scan will show areas of fixed hypoperfusion indicating a myocardial infarction and the echocardiogram will evaluate wall motion abnormalities from myocardial scar. If significant Q-waves are found but there is no evidence of a prior myocardial infarction or significant coronary disease, the aviator is returned to unlimited flying duties.

#### NONSPECIFIC ST AND T-WAVE ABNORMALITIES:

Hiss and Lamb (1) reported that 1.2% of initial electrocardiograms in aviators demonstrated nonspecific T-wave changes. They did not discuss the incidence of nonspecific ST segment abnormalities. In an asymptomatic population, nonspecific ST and T-wave abnormalities seen as a serial change double the predictive value of screening treadmill tests for coronary artery disease (13). If a resting electrocardiogram shows nonspecific ST and T-wave abnormalities as a serial change from prior normal studies, a treadmill exercise tolerance test should be performed. If the treadmill test is normal, no further evaluation is required. If the treadmill test is abnormal, a complete ACS evaluation is required. Care should be taken to insure that the treadmill test is performed in a fasting state. In addition, baseline, supine, standing, and posthyperventilation ECGs should be obtained as a routine portion of the treadmill test. If these maneuvers cause significant ST and T-wave abnormalities, these tracings should become the new baseline from which to measure additional ST segment depression during exercise.

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## ECHOCARDIOGRAPHIC SCREENING OF AIRCREW CANDIDATES

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Military pilot training is expensive for all NATO countries, and screening techniques which detect medical conditions at selection which might later result in grounding or operational restriction of trained pilots are generally cost-effective. Although a careful physical examination and electrocardiogram will detect most disqualifying conditions, there are a number of structural cardiac abnormalities which may be missed by these standard screening measures. These include the following:

Mitral Valve Prolapse

Bicuspid Aortic Valve

Hypertrophic Cardiomyopathy

Left Ventricular Hypertrophy  
Diastolic Dysfunction

Regurgitant Valves

Aortic  
Mitral  
Tricuspid  
Pulmonic

Significant Stenosis

Aortic  
Pulmonic  
Mitral

Other Congenital Lesion  
e.g Ebsteins anomaly

Only four of thirteen NATO aeromedical agencies polled by questionnaire reported that an echocardiogram is included in the routine initial screening of aircrew candidates (see paper 1 in this monograph). The detection of disqualifying or limiting cardiac abnormalities in trained aircrew is a clear argument in favour of screening, but it is really the incidence of such abnormalities detected in aircrew candidates which determines the cost-effectiveness of the procedure.

The Canadian Forces initiated M-mode and 2-D echocardiographic screening of aircrew candidates in 1985, and in 1989 upgraded the screening to include colour flow mapping and doppler. All candidates for pilot training are first screened at a local recruiting center with a clinical examination and standard ECG. Successful candidates undergo second level screening at a single central location at the Medical Assessment Section at DCIEM in Toronto concurrent

with aircrew selection screening at the Canadian Forces Aircrew Selection Center.

In table 1, the echocardiographic findings in 2767 candidates screened over a period of 55 months with conventional M-mode and 2-D echocardiography but without doppler are shown.

Table 1	No.	%
Mitral Valve Prolapse	119	43
Bicuspid Aortic Valve	68	2.5
Aortic sclerosis/stenosis	6	<1
Hypertrophic cardiomyopathy	4	<1
Left ventricular hypertrophy	2	<1
Ventricular septal defect	1	<1
Aortico-ventricular tunnel	1	<1
<b>TOTAL</b>	<b>201</b>	<b>7.2</b>

In Table 2, the findings in 1476 candidates screened over a period of 34 months with expanded screening to include colour flow mapping and doppler are shown.

Table 2	No.	%
Mitral Valve Prolapse	59	4.0
Echo equivocal	8	
Clinically Positive		
Bicuspid aortic valve	14	0.9
No aortic regurgitation	5	
Slight/mild aortic regurg	7	
Moderate aortic regurg	2	
Aortic regurgitation	34	2.3
Normal aortic valves	19	
Bicuspid aortic valve	9	
Left vent hypertrophy	5	0.3
Assym. septal hypert.	2	0.1
Atrial septal defect	1	0.1
Endocardial cushion defect	1	0.1
<b>TOTAL</b>	<b>115</b>	<b>7.8</b>

The overall incidence of disqualifying echocardiographic findings in 4243 candidates screened over 5.5 years was 7.4%. The vast majority of

these are detectable with a simple m-Mode/2-D echo. None of these abnormalities had been detected on initial screening with a clinical examination and electrocardiogram, although some were confirmed on clinical examination by the Internist at the time of second level screening.

These findings are likely representative of what would be expected in other NATO countries carrying out echocardiographic screening of aircrew candidates. In Canada, the echocardiographic screening is performed by a certified civilian technologist. The echocardiograms are reviewed and reported by a military Internist attached to the Medical Assessment Section. The estimated cost per screening echocardiogram based on 10% of the Internist's time and 75% of the technologist's time (the remainder is for research and clinical assessments) is \$72.00 Cdn. The amortized 10 year cost of equipment with upgrades and maintenance contract is approximately \$38,000 Cdn per year. Based on 80% utilization for aircrew screening this is approximately \$60.00 per aircrew screening study. The total cost per study is therefore estimated at \$142.00 Cdn

The cost of screening 1476 candidates with echo and colour flow is estimated at \$210,000 to detect 115 disqualifying abnormalities, or \$1820 each. Estimating the cost of pilot training to operational readiness at \$750,000 Cdn (higher for fighter pilots), this represents a saving of approximately 30 million dollars per year. This of course assumes that all candidates screened out would eventually require grounding; this is obviously not the case, but even if 10% were eventually grounded, the savings are still substantial.

Echocardiographic screening of aircrew candidates for structural cardiac abnormalities is cost effective and is recommended for all NATO countries. Screening with M-mode and 2-D echocardiography will detect the vast majority of abnormalities. The more comprehensive assessment with colour flow and doppler permits detection of a small additional number of regurgitant (mainly aortic) valves.

The aeromedical significance of the various structural cardiac abnormalities including mitral valve prolapse is the subject of the following papers by Dr. Celio and Air Commodore Hull.

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# **ECHOCARDIOGRAPHIC FINDINGS IN TRAINED AIRCREW - THE EFFECT OF +Gz ON CARDIAC STRUCTURE (WORKING GROUP 18)**

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During the AGARD conference "Medical Selection and Physiologic Training of Future Fighter Aircrew" in April 1985, Dr H. Ille presented a paper on echocardiography in Mirage 2000 pilots (1). In this study, 32 Mirage 2000 pilots and 34 transport pilots underwent echocardiography in order to evaluate the possibility of cardiac changes occurring because of high performance flying. The authors found a statistically significant increase in left atrial size and left ventricular septal thickness. They also felt that there was a very significant difference in right ventricular dimensions. The mean right ventricular size for the transport pilots and the Mirage pilots was 13.265 mm and 16.750 mm, respectively. They felt that 8 of the Mirage 2000 pilots had dilated right ventricles whereas only one of the transport pilots had an enlarged right ventricle.

Although the cause of this apparent difference could not be determined by the study, the presence of right ventricular dilatation in high performance pilots raised a significant occupational concern among the NATO countries. Although this may simply be an artifact of the small sample size or a result of the inherent difficulty in obtaining right ventricular dimensions, the possibility that this represented a true occupational hazard was seriously considered.

In order to determine the significance of this finding, a larger study was undertaken by AGARD. This study is described in the AGARD Advisory Report Number 297, "Echocardiography in NATO Aircrew". The intention is to perform a large cross-sectional study comparing the echocardiographic findings obtained on pilots flying high sustained G aircraft with non high sustained G pilots (tanker, bomber, transport, helicopter pilots). The goal is to obtain 500 matched pairs for comparison. A detailed history concerning medical problems, cigarette smoking, and exercise is to be included. Exercise is of specific concern since exercise is known to affect cardiac dimensions. These studies are to be performed by all participating NATO countries. Echocardiographic data is entered into a database program specifically designed for this project. All echocardiographic data including a specified percentage of tapes are forwarded to the United States Aeromedical Consultation Service at Brooks Air Force Base, Texas, for quality control, archiving, and analysis.

At this time, a total of 870 studies have been submitted by all participating countries. A breakdown of study types submitted by each

**TABLE 1**  
**TYPES OF STUDIES SUBMITTED**

<u>COUNTRY</u>	<u>M-MODE</u>	<u>2 D</u>	<u>DOPPLER</u>	<u>TOTAL</u>
GREECE	200	200	200	200
SPAIN	71	1	9	71
ENGLAND	43	43	43	43
BELGIUM	331	74	60	331
CANADA	42	42	42	42
USA	62	62	62	62
FRANCE	76	0	76	76
NORWAY	<u>45</u>	<u>45</u>	<u>45</u>	<u>45</u>
TOTAL	870	475	537	870

**TABLE 2**  
**STUDIES BY PILOT TYPE AND COUNTRY**

	High Sustained <u>G Aircraft</u>	Nonhigh Sustained G Fighter <u>Aircraft</u>	Nonhigh Sustained <u>G Aircraft</u>
GREECE	37	118	0
SPAIN	31	6	13
ENGLAND	3	0	30
BELGIUM	7	134	39
CANADA	7	7	4
USA	1	14	19
FRANCE	76 Studies - Incomplete flying data		
NORWAY	<u>41</u>	<u>0</u>	<u>4</u>
TOTAL	127	279	109

studies obtained by pilot type and country. In total, we have obtained 127 pure high sustained G pilots, 109 non high sustained G pilots, and 279 fighter pilots in non high sustained G aircraft.

A complete analysis of data obtained by September 92 was presented at the last AGARD Working Group Meeting. All echocardiographic parameters including right and left ventricular dimensions were examined. Based on the data received at that time, there were no parameters that showed statistically significant differences between each pilot group.

This study is still progressing in the data collection phase. The current plan calls for one more year of data collection prior to final analysis. Once this study is concluded, we will be able to make a more definitive statement regarding the cardiac consequences of high performance flying. If significant differences in cardiac dimensions or function are identified, further studies will be designed in order to identify the etiology of these changes. If there are no significant differences in these cardiac parameters, additional echocardiographic studies will not be necessary.

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## LEFT VENTRICULAR HYPERTROPHY AND ATHLETE'S HEART

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Left ventricular hypertrophy (LVH) means literally, overgrowth of the left side of the heart. However the term is generally limited to an abnormal increase in the mass of the left ventricular heart muscle. In pathological terms, this means an increase in the size of the cardiac myocytes as opposed to hyperplasia, an increase in their number. In common parlance, any thickening of the left ventricular wall tends to be described as LVH; this is incorrect where the thickening is due to increase in the size or number of cells other than myocytes, such as fibroblasts, or to abnormal deposits, e.g., amyloid. LVH may be present with normal wall thickness in an enlarged ventricle, for example in volume overload. In health, left ventricular mass is directly related to stature and to body weight, and increases steadily with age (1,2) so a single standard (maximum) left ventricular wall thickness for all ages, both sexes and all bodily configurations must be inappropriate. However, normative standards incorporating these sources of variability are rarely employed.

Hypertrophic cardiomyopathy (HCM), originally described by Teare (3) in 1958, is an abnormal condition of the heart muscle characterised by a hypertrophied and non-dilated left (and/or right) ventricle in the absence of a cardiac or systemic cause for LVH (4). (Sometimes, by coincidence, there may be another potential cause for LVH, e.g., hypertension; and rarely, usually late in the course of HCM, the left ventricle may become dilated.) Disarray, often gross and extensive, of the heart muscle fibers is the hallmark of the condition (3) but may be found to a more limited extent in other cardiac conditions and even in normal hearts (5). HCM is the most commonly familial, behaving as a Mendelian autosomal dominant characteristic, (6) but apparently sporadic cases (mutations) are common (7). It may be completely asymptomatic, but chest pain, often exertional, effort dyspnoea, palpitations and syncope are common. These symptoms, and high grade ventricular arrhythmias, are ominous, but even in their absence, sudden death occurs in half or more of all cases (8); the attrition rate is generally around 2-3% per year in large series (7). Older patients are prone to atrial fibrillation and cardiac failure (2). No treatment has been shown to prolong life. The prevalence of the disease is about 20 per 100,000 of the population (4).

LVH is important in aeromedical practice because of its apparent or actual presence in ostensibly healthy young and middle aged people, especially men. ECG voltage criteria (9) for LVH are found in the ECG's of over 30% of RAF crewmen at their routine flying physical examinations. Clearly, the great majority of these ECG's represent physiological variation.

However in young aircrewmen or recruits in their twenties, in whom voltage increase are commonest, repolarization abnormalities are also commonly seen and may simulate early "type B" LVH or the left ventricular strain pattern. Many of these individuals are in good physical training, often for endurance sports, and the ECG changes may represent the normal physiological response to the repetitive exercise stress, that is, physiological LVH, a feature of athlete's heart. Although other causes of LVH (eg, systemic arterial hypertension, unrecognized aortic valve disease or ischemic heart disease) may rarely be present in an asymptomatic aircrewman, it is much more usual for no underlying pathological basis to be detected. The differential diagnosis is then between physiological LVH and hypertrophic cardiomyopathy. The importance of this distinction in aviation clinical practice can hardly be exaggerated. HCM may cause (and quite often presents with) sudden death, particularly during vigorous physical exertion. Syncope, usually due to ventricular tachycardia or fibrillation, possibly to asystole, is quite common. Less severe symptoms (chest pain, palpitations) may be distracting and therefore a hazard to the flying task. Though specific details of the effects of flying stresses in HCM are not available, high G forces may cause arrhythmias and marked changes in cardiac cavity dimensions even in healthy aviators. Drugs used for HCM (eg, beta-blockers and anti-arrhythmics) may introduce added hazards in the flying environment.

The Table shows many features which may help to distinguish physiological LVH from HCM. It is clear that there are many features of HCM, which, if present in some numbers, are virtually diagnostic (though none, in isolation, is unique to HCM). However the usual aeromedical situation involves an apparently healthy, asymptomatic and athletic young person with a negative or incomplete family history and non-specific physical signs. The echocardiogram shows moderate LV wall thickening, say 1.5-1.7 cm for the IV septum in systole. Other echo findings are normal or equivocal. Sometimes suboptimal images have been obtained, or confidence is reduced by an unusual heart position entailing non-standard probe positions and echo views. Though there is little if any persuasive evidence for HCM, the diagnosis can not be excluded with confidence.

In earlier years it was the usual practice to require a repeat echo study after a period of enforced physical inactivity (12). In physiological LVH, some reduction in LV wall thickness occurs within a few weeks, but the improvement may be too slight to be convincing. Full return to normality may take 3-6 months, with very considerable inconvenience to all concerned,

especially if the subject is a top-flight competitive athlete. The financial penalty to the prospective employer and employee is substantial whilst a promising recruit may lose patience and choose an alternative career.

A different approach is proposed by Lewis and co-workers (15) who compared the echo and doppler characteristics of 3 groups; athletes, untrained healthy controls, and young patients with fairly mild HCM. LV diastolic cavity size was greater in athletes than in patients with HCM but otherwise the echo studies in the three groups were rather similar. However, LV filling characteristics in HCM differed quite markedly from the normal values obtained in both athletes and controls. The mitral valve doppler waveform in HCM showed a relatively lower E peak, a

much reduced E:A ratio, and a significantly shallower E-F slope.

The study involved small numbers and there was a little overlap between HCM and the athletes/normals in the measurements mentioned, but overall the differences were impressive. This work is consistent with other findings of abnormal diastolic dysfunction in HCM (16) and, if confirmed, offers a promising method for distinguishing the numerous cases of physiological LVH from the few with HCM in the aircrew and pilot candidate population. Indeed, diastolic dysfunction (by echo or scintigraphy), if detected in an individual with LVH unexplained by any other cause, gives powerful support to the diagnosis of HCM.

TABLE  
DISTINGUISHING PHYSIOLOGICAL LVH AND HCM

		PHYSIOLOGICAL LVH	HCM
Symptoms.	Chest Pain Palpitations Syncope	Rare(19)	Common
Positive family history			
Signs.	Jerky Pulses Systolic heart murmur Triple rhythm	No Common Common (3rd HS)	Common Common Common (4th HS)
Abnormal ECG.	Voltage LVH ST-TWCs Q-waves Dysrhythmias	Common (5) Quite common (20) Rare Common (5.,19)	Common Common Common Common
Chest x-ray.	Prominent LV Mild cardiomegaly	Common Sometimes	Common Sometimes
Imaging.	Increased LV wall thickness IV septum: post wall ratio LV cavity - size - shape Ejection fraction (22) Fractional fibre shortening Atrial dimensions Mitral valve - regurgitant - systolic antr mvt Aortic valve - mid-systolic closure Septal endocardial plaque Diastolic function Ventricular pressure gradient Response to CVS stressors Endomyocardial biopsy	Mild/mod Normal Normal or increased Globular or normal Low -normal Low-normal Normal Often (slight) No No No Normal Rare Damped (23) Normal	Mild/severe Often increased Normal or reduced Crescentic or normal High-normal or increased High-normal or increased Often enlarged (21) Often (moderate) Often Often Often(21) Usually abnormal (10) Common Exaggerated Often abnormal

A definite diagnosis of HCM is disqualifying for entry to flying training. If the condition is diagnosed in a trained aviator, he should be permanently grounded. This draconian disposal is based on the natural course of the disease, as outlined above. Although certain features - a family history of sudden death in childhood or young adult life, a personal history of symptoms especially syncope, and documented high-grade ventricular arrhythmias - are strongly predictive of an early fatal outcome, there are no positive features that would select patients with a good prognosis. A few authors (13,17) claim to have identified a group with a good prognosis, but these are mainly older patients; others (18) have found no reduction in mortality in similar groups. Unheralded loss of consciousness, e.g., from ventricular tachycardia, or sudden death, can occur in totally asymptomatic individuals with apparently mild or localized hypertrophy (there is, in fact, evidence of generalized disease even in patients with apparently localized lesions)(10). Despite these observations, a few individuals with HCM survive to retirement and even to old age without development of serious symptoms. Based on this, a very few aircrewmembers with asymptomatic nonobstructive HCM have been returned to restricted flying duties. The long term outcome is awaited with interest.

By contrast, physiological LVH, in the absence of symptoms, is compatible with unrestricted flying duties. Other forms of LVH are generally secondary to diseases which themselves will lead to flying restrictions or grounding. Occasionally mild early LVH is recognized in a hypertensive and regresses to normal with successful antihypertensive treatment compatible with flying duties. Provided there is no evidence of ischemic or other heart disease, such individuals may be able to return to flying whilst their hypertension is controlled on treatment.

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## AORTIC VALVE DISEASE

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The aortic valve, like the pulmonary valve, forms early in foetal cardiac development soon after the fusion of the 2 bulbar ridges which thus become a septum dividing the primitive bulbus cordis into the aortic and pulmonary trunks. Two cusps of each valve arise from the fused ridges, whilst a third cusp is formed from accessory ridges in each outflow tract. The normal arrangement is of symmetrical semilunar 3-cusped valves in aorta, and pulmonary trunk, but variations are common. A bicuspid aortic valve is present in 1-2% of adults; (1) a unicuspid or quadricuspid valve is much rarer. Bicuspid valves are 4 times commoner in men than in women. Lesser degrees of asymmetry are so common as to be the rule; in one series (2), only 16% of normal aortic valves were perfectly symmetrical in the sense that all 3 cusps were within 5% of each others dimensions; in 33% of valves, all 3 cusps differed from each other by more than this amount. The significance of these minor degrees of asymmetry, particularly with regard to the later development of aortic valve disease, is unknown. Congenital aortic valve abnormalities are common associations of other types of congenital heart disease, notably of coarctation of the aorta and ventricular septal defect.

Aortic valve lesions are asymptomatic in most young people; because of this, and of male preponderance, congenital aortic valve disease is quite common in applicants for flying training; as abnormal physical signs are often trivial or absent, acceptance into aircrew training is probably the rule and the abnormality is recognized only later.

Although, overall, aortic stenosis is commoner than aortic regurgitation in bicuspid valves (3), a significant stenosis is rather rare in young adults and regurgitation is much commoner. However, neither may be present. A systolic murmur is often quiet and has characteristics to the very similar to those of the innocent flow murmur heard in many young people; being due to the same cause, turbulence in the aortic outflow tract. The diastolic murmur of aortic regurgitation (AR) is often excessively quiet, even with the usual positioning and respiratory manouevres; but there is sometimes a clue in the rather emphatic unsplit quality of the aortic second sound. Indeed, in many cases of bicuspid valve there is a very characteristic cadence, with a normal first sound, early apical and basal ejection sound or click, and single second sound - "Tennessee". The chest x-ray and ECG are almost always normal, but echocardiography, in the large majority where good 2-D images can be obtained, is usually diagnostic (4). The aortic valve closure line is nearly always eccentric on the long-axis parasternal view, and the

short-axis view may show the typical oblique "fish-mouth" configuration of the bicuspid valve during ventricular systole, or at least a single unbroken slightly curved diagonal closure line, as opposed to the usual symmetrical "inverted Y" tri-radiate commissure line, in diastole. Colour doppler reveals diastolic regurgitation when present, and often systolic turbulent flow although, as already noted, actual stenosis is exceptional. Associated congenital abnormalities (coarctation, ventricular septal defect) are unusual in ostensibly healthy young people; ventricular wall and cavity dimensions will be normal.

Candidates for flying training with a bicuspid aortic valve, even without AR or AS, should be refused. There is little immediate risk but the prognosis is too uncertain. The chances of developing infective endocarditis are appreciable despite antibiotic prophylaxis, which may well be neglected during military exigencies; morbidity and mortality of infected endocarditis are high. The valvular disease, in any case, tends to progress, with increasing and eventually haemodynamically significant AR, which will necessitate flying restrictions and later grounding. Degenerative changes in the valve cusps (fibrous sclerosis progressing to calcific deposits, seen at first as echodense sessile nodules on ultrasound) lead to deformity, scarring and stenosis. Various degrees of hear block may occur. Fine judgment is required in the timing surgery (usually valve replacement, a procedure with appreciable mortality). Artificial or tissue valves are incompatible with most types of flying. Associated abnormalities such as idiopathic aortic root dilation and prone-ness to aortic dissection, may become apparent only later (3).

The Canadian Armed Forces screen aircrew recruits echocardiographically and are thus much more likely to detect aortic lesions. An occasional finding is mild (1.7%) or more marked (0.2%) AR in the presence of an apparently normal 3-cusped aortic valve (5). The AR is most often minor or trivial and, (apart from the common physiological regurgitation seen in the other heart valves in healthy young people (6) the rest of the examination is normal. Some cardiologists report never seeing AR in the presence of a normal valve and healthy heart (6); others, however, confirm the Canadian Armed Forces' experience (7,8). The problem is whether such applicants should be accepted for flying training.

The policy in the RAF is that they should not, though this decision is not universally accepted (5). The RAF view is based largely on uncertainty as to the long-term outcome, with the general experience that AR

of any type tends to deteriorate with time. Infective endocarditis sometimes seems to have arisen on a healthy valve; has this valve in fact been mildly regurgitant, causing trauma to the cusp margins which provides a nidus for infection? Echo is an imperfect method for defining minor lesions (4), and these valves may be asymmetrical or the site of a degenerative process (connective tissue disorder such as myxomatous degenerative, Ehlers-Danlos or Marfan's syndrome). Some other cause of AR may be operating, e.g., ankylosing spondylitis, Reiter's syndrome, rheumatic endocarditis of syphilis (9).

Not infrequently, asymptomatic AR is discovered in a trained aviator in his third or fourth decade of life. A bicuspid or asymmetrical valve is a common finding, but an extensive work-up is needed to exclude other causes, establish the normality of the heart in other respects, and determine the aircrewman's response to exercise and (if possible) +Gz stress in the centrifuge. Most cases can be investigated non-invasively. Where the AR is mild, with no haemodynamic effect, and no AS or other significant abnormality, the individual may often be returned to unrestricted flying duties subject only to as-required antibiotic prophylaxis and regular specialist follow-up. Many can continue a flying career for a number of years, but as the disease progresses, radiological, ECG and echo evidence of haemodynamic (volume overload) and other effects become evident and flying restrictions, eventually grounding, becomes necessary. Minor degrees of aortic stenosis (e.g., a gradient of 10-20 mm Hg on doppler) are compatible with flying, but again, progression, which is the rule (10), will disqualify.

**Conclusion.** Significant aortic valve disease is quite common in other wise healthy young and middle-aged men but to a much lesser extent in women. The recrudescence of rheumatic fever may increase these numbers. Aortic stenosis which is more than minor, and haemodynamically significant aortic regurgitation, are incompatible with control of aircraft. The availability of echocardiography with colour doppler, increasing used for screening aircrew candidates, will in future lead to the recognition of much larger numbers of healthy individual with minor and apparently trivial, possibly developmental anomalies.

Appropriate decisions on the acceptance or rejection of these individuals for flying duties must depend on the results of long-term studies of the natural history of these anomalies. At present, the discovery of bicuspid aortic valve, or even of mild AR, should be considered disqualifying for military pilot selection and training.

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## AEROMEDICAL IMPLICATIONS OF MITRAL VALVE PROLAPSE

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Mitral valve prolapse (MVP) is the most common cardiac valve disorder in the general adult population. Although the prevalence has been estimated at between 4% and 21% the true prevalence is dependent upon the specific population evaluated and the diagnostic criteria applied. For the adult male population of aircrew age, the prevalence is probably between 4% to 7%. Although the prognosis of individuals with MVP is generally good, rare complications do occur which include sudden death, infective endocarditis, stroke, transient ischemic attacks and progressive mitral regurgitation. The following discussion will review the diagnostic criteria as well as the probable risk of each reported complication.

Since rare complications do occur with MVP, accurate diagnosis and follow-up is important. The diagnosis is routinely made on the basis of either physical exam findings or the results of echocardiography. On physical exam, the typical features are midsystolic clicks. These move with respect to the first and second heart sounds in response to maneuvers that change left ventricular size relative to mitral valve size. The midsystolic clicks classically move earlier into systole with standing, sitting or other maneuvers that reduce ventricular size. The midsystolic clicks move later into systole with maneuvers that increase left ventricular size such as squatting. The late systolic murmur of MVP occurs just after the midsystolic click. The beginning of the late systolic murmur also moves with maneuvers in the same fashion as the midsystolic clicks. Variations in auscultatory findings from one physical exam to the next are a classical feature of MVP. This phenomenon is probably related to minor variations in left ventricular size due to changes in volume status from one physical exam to the next.

Although MVP may be diagnosed by classical auscultatory findings, a certain percentage of individuals with documented MVP may have a completely normal physical exam. Mitral valve prolapse may also be diagnosed by typical findings on echocardiography. The M-mode echocardiogram may show mid to late posterior systolic motion of the mitral valve. Mitral valve prolapse is diagnosed by at least 2 mm of late systolic posterior motion of the mitral valve behind the line connecting the closure and opening points of the valve. Mitral valve prolapse is also diagnosed if there is at least 3 mm of holosystolic prolapse. Two-dimensional (2D) echocardiography will show

systolic motion of the mitral leaflets into the left atrium behind the mitral annulus. This is diagnosed only on the parasternal long axis view. In the past, MVP was diagnosed on the apical four chamber view. A study by Warth et al., found a 34% prevalence of mitral valve protrusion across the mitral annular plane in a group of adolescents in the apical four chamber view (1). A later study by Levine et al., demonstrated that the mitral valve had a "saddle" shape and normally appeared prolapsed on the apical four-chamber view (2). For this reason, MVP should only be diagnosed on the parasternal long axis view.

Although MVP will be expected in a large number of pilots from any nation, its real impact on flying safety remains controversial. The least controversial complication for MVP is progression to severe mitral regurgitation. Mitral valve prolapse is now considered to be the most common cause of severe isolated mitral regurgitation requiring mitral valve surgery. Studies have shown that MVP is the cause of severe pure mitral regurgitation in 38 to 64% of patients. Wilken et al., calculated the life-time risk for needing mitral valve replacement for patients with MVP at approximately 4% among men and 1.5% among women (3). Devereux et al., estimated the life-time risk for mitral valve replacement at 5.5% for men and 1.5% for women (4). Although progression of mitral regurgitation can be followed over time and rarely presents with sudden incapacitating symptoms by itself, the increased risk of severe mitral regurgitation and valve replacement reduce the likelihood of a full flying career and adds an extra burden to the medical resources of any air force.

The risk of infective endocarditis also appears to be increased for individuals with MVP. For the general population, the average probability for developing infective endocarditis is one case per year for 20,000 persons (5). Devereux et al., estimated that one patient would develop infective endocarditis for every 1,920 patients with MVP who had a late or holosystolic murmur of mitral regurgitation (5). This compared with one case per 21,950 without a murmur of mitral regurgitation. They also calculated the risk of infective endocarditis at one case per 3,640 affected men and one case per 2,930 persons 45 years of age or older with MVP. Although there is evidence that endocarditis is more likely in an individual with a murmur, Devereux also demonstrated that the murmur on physical exam is a highly variable finding (6). Since the murmur in

MVP may not be present on every examination, the Aeromedical Consultation Service (ACS) recommends endocarditis prophylaxis for all aviators with MVP.

The risk of stroke is also reported to be increased in patients with MVP. Sandok et al., reported the results of a prospective study of 1,138 individuals with MVP (7). There were cerebrovascular accidents reported in 40 cases. Twenty-six of these 40 had no other identifiable cause for their CVA. One-third of this group were men and the mean age was 48 years of age. The prevalence of stroke in the 22 to 44 year age group was 3%. The prevalence of CVA was 4-5 times greater in the MVP group than that expected of the general population. Barnett et al., also reported an increased risk of stroke of approximately six-fold for women under the age of 40 with MVP (8).

The association of MVP with sudden death remains a controversial issue in the medical literature. Mitral valve prolapse has been found as the only cardiac abnormality in survivors of cardiac arrest and cases of sudden death. Duren et al., performed one of the few prospective long-term follow-up studies of idiopathic mitral valve prolapse in 300 patients (9). Patients were eliminated from the study if they had a history of rheumatic fever, ischemic heart-disease, cardiomyopathy, congenital heart defects, perimyocarditis, right ventricular dysplasia, Marfan's syndrome, hypertension, cardiac trauma, increased QT interval, or electrocardiographic signs of pre-excitation. Sudden death most likely due to ventricular fibrillation occurred in three patients, documented ventricular fibrillation was identified in two patients, and ventricular tachycardia developed in 56 patients. Sudden death occurred in two men, ages 27 and 70, and one woman, age 53. The 27-year-old patient died suddenly and unexpectedly from ventricular fibrillation. After successful defibrillation, he was found to have short episodes of ventricular tachycardia on 24-hour Holter monitoring. Angiography was normal. He was treated with alprinolol and diphenylhydantoin but had sudden death six months later. The two other patients that died suddenly had significant mitral regurgitation. A fourth patient, a 34-year-old man, experienced ventricular fibrillation but was successfully resuscitated. Extensive cardiac evaluation showed MVP without mitral regurgitation or other significant organic heart disease. He was placed on antiarrhythmic therapy, and a 24-hour Holter continued to show asymptomatic brief runs of ventricular tachycardia. Although this is a highly selected population because of their referral to a tertiary medical center, there is a strong suggestion that MVP was responsible for these events even in the absence of severe mitral regurgitation.

A recent review by Kligfield and Devereux examined the literature regarding MVP and sudden death (10). Davies et al., reported 13 cases of unexpected sudden death associated with only

MVP during a 5-year period (11). Nine of these cases were associated with significant mitral regurgitation. Duren et al., reported a similar finding with the association of sudden death with MVP patients with significant mitral regurgitation (9). Based on the analysis by Kligfield, the annual risk of sudden death in patients with MVP without significant mitral regurgitation was 1.9 cases per 10,000 or approximately 0.02% per year. Their analysis, however, indicates far greater risk for those patients with MVP and significant mitral regurgitation. Their analysis suggests an annual risk of sudden death in this population at between 94 and 188 cases per 10,000 or 1 to 2% per year. Although this analysis is supported by some studies, reported cases of patients with MVP resuscitated from sudden death were not found to have a high prevalence of severe mitral regurgitation. Although some evidence suggests that severe mitral regurgitation represents a cofactor predictive of sudden death in MVP, sudden death clearly can occur in individuals without significant mitral regurgitation.

Another cofactor that may be predictive of a high risk population is mitral leaflet thickening. Nishimura reported that patients with mitral valve prolapse with leaflet thickening had the highest risk of complications (2). Marks et al, found that 62 of 319 patients with leaflet thickening with mitral valve prolapse required mitral valve replacement or developed endocarditis or severe mitral regurgitation, whereas, only 1 of 137 patients with thin leaflets developed a complication (13). There were no sudden deaths in this group and the incidence of stroke was the same with either normal or thickened leaflets.

In summary, the medical literature supports a small but definite increase in risk in patients with mitral valve prolapse for stroke, infective endocarditis, progression to severe mitral regurgitation, and sudden death. Because of this, the USAF disqualifies pilot applicants with MVP from training. Aviators found to have MVP after training undergo complete evaluation at the Aeromedical Consultation Service. This includes a complete cardiac evaluation and a medically monitored centrifuge ride if they continue to fly high performance aircraft. Asymptomatic aviators without a history of complications and found to have normal cardiac evaluations are returned to unrestricted flying duties. These aviators are evaluated every 3 years.

Aviators with supraventricular tachycardia (SVT) return to full flying duties under the guidelines of the SVT Study Group. At the present time, however, aviators with ventricular tachycardia are disqualified from all flying duties. Since the mechanism of sudden death in MVP appears to be ventricular fibrillation, our obvious concern is that even brief runs of ventricular tachycardia in these aviators may impart a greater risk in this subgroup. Although this has not been definitely established,

there have been no studies that have followed a sufficient number of otherwise asymptomatic individuals with ventricular tachycardia and MVP to establish the real risk.

We are currently undertaking a review of all aviators seen at the ACS with ventricular tachycardia. Of the 193 aviators, 31 were diagnosed as having MVP. One aviator with MVP had sudden death at age 53. Autopsy showed only MVP and no other evidence of heart disease. A second patient had frequent episodes of presyncope and no other evidence of heart disease. He had recurrent non sustained (up to 20 beats) polymorphic ventricular tachycardia. Although the results of our study are still preliminary, we feel that our experience and the medical literature supports sufficient concern over the possibility of sudden death in individuals with ventricular tachycardia and MVP to preclude these aviators from continued flying duties.

The ultimate disposition for all aviators with MVP will rest on the results of future long-term prospective studies. Most studies in the medical literature are affected by significant selection bias since most asymptomatic individuals with MVP are probably never diagnosed. Most patients that appear in medical studies such as the paper by Duren et al, were referred to a major medical center. Their population probably represents one extreme in the prognosis of a group of patients with MVP. Aeromedical policy for aviator with MVP may change as long-term studies of incidentally found individuals with MVP are published.

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## CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Chronic Obstructive Pulmonary Disease (COPD) remains a common cause of illness and death in many Western countries and is an increasing problem in developing nations. Although COPD is declining slowly in the UK, it still causes 15000 deaths annually and is responsible for 10% of all working days lost through illness(1). This is despite improved working conditions, much reduced atmospheric pollution and a decreased tobacco consumption. In the USA, COPD is the fifth commonest cause of death, causing 57000 deaths per year. It is estimated that 81.5% of this toll is due to cigarette smoking(2). Clinically apparent disease is largely confined to middle-aged and elderly people, but many young cigarette smokers can be shown to have early evidence of airways disease if adequately investigated.

Two main types of COPD are seen, chronic bronchitis and emphysema, though patients may show features of both disorders. Chronic bronchitis is defined (3) as the production of mucoid sputum on most days for at least 3 months during 2 consecutive years. Recurrent respiratory infection is increasingly common as the disease progresses. Stopping smoking may, especially early in the disease, arrest or slow its progression. Otherwise deterioration is remorseless. Apart from variable rhonchi, physical signs are often slight till the onset of cor pulmonale, that is failure secondary to the broncho-pulmonary disease. Finger-clubbing, raised venous pressure, fluid retention, evidence of right ventricular hypertrophy, hypercarbia with respiratory acidosis and raised intracranial pressure and eventually hypoxaemia are the main features; despite remissions cor pulmonale is usually fatal within a few years.

In chronic bronchitis, the large airways show marked enlargement of the mucous glands (4), increase in goblet cells, and loss of cilia (2). There is often hyperplasia of the smooth muscle of the central airways. More peripherally, the main features are inflammation, bronchiolar mucous plugging, peribronchiolar fibrosis.

Emphysema is defined pathologically as a permanent abnormal enlargement of the air spaces (acini) distal to the terminal bronchioles. At least 4 distinct types are recognized pathologically (3) though clinical distinction is often impossible and may not be important. Histological features include destruction of the peribronchiolar alveoli and small arteries, and increase in neutrophils and activated macrophages, and increase amounts of immunoglobulins A and G. Clinically, emphysema is rarely apparent until the disease is well established. Effort dyspnoea is usually at first attributed to

overweight or unfit. Generalized reduction in air entry is at first subtle, and added sounds quite unusual. The classical features of a barrel chest and reduced cardiac and hepatic dullness to percussion are late signs, as are the radiological features (narrow mediastinum, flattened diaphragm, transradiant lung fields, cysts).

Emphysema is overwhelmingly caused by cigarette smoking, which also greatly aggravates the disease in the few cases where there is another underlying aetiology. The Royal College of Physicians of London (5) estimates that smokers of 15 to 24 cigarettes per day are 25 times more likely to die of emphysema than lifelong non-smokers. Quitting smoking, early in the disease, may slow or arrest its progression. Unfortunately, once the disease is clinically evident, steady deterioration is the rule whatever measures are taken. Progressive dyspnoea, at first exertional, eventually at rest, is the main symptom. Though exertional hypoxaemia is present, cyanosis is unusual ("pink puffers"); carbon dioxide retention and cardiac failure are unusual and late.

Alpha-one antitrypsin deficiency (6) (protease inhibitor deficiency) is a disorder which, in its homozygous form, strongly predisposes to the development of emphysema. (The commoner heterozygous form of the disorder rarely causes disease.) The homozygous disease is very unusual, accounting for fewer than 1% of all cases of emphysema, and occupational screening is rarely considered worth-while.

Whether bronchial hyper-reactivity plays a part in individual predisposition to COPD has long been disputed(7). Although the pathological damage seen in COPD is clearly irreversible, an element of bronchospasm is quite often present, and bronchodilators may be helpful.

Primary prevention of COPD in aircrew is clearly the best option, and depends on avoidance of tobacco smoking, especially of cigarettes. Only 30% of the adult UK population now smokes, and government policy aims to reduce this to 21% by the year 2000(8). Unfortunately young women, increasingly recruited to aircrew duties, show a tendency to increased numbers of smokers. Smoking is much commoner in some countries; in the Spanish Air Force, for example (9), as recently as 1984 61% of aircrew were smokers, reducing to 47% by 1992. Of Spanish pilots found to have coronary disease, 87.5% were heavy cigarette smokers(10). It is known that most adult smokers acquire the habit in childhood, and in this regard the figures are more encouraging; e.g., only 30% of Spanish Air Force cadets are smokers (9) whilst in the

UK, where there is a steep gradient in smoking based on educational standards, fewer than 5% of all RAF aircrew recruits are cigarette smokers. A few civil airlines will not engage pilots who are smokers. I know of no military forces which does the same, perhaps because of the likelihood of false declarations. RAF regulations state that "non-smoking candidates will be preferred".

Although early or mild COPD is usually asymptomatic, and individuals with moderate disease may have little handicap, there are strong aeromedical reasons for restricting the employability of aircrew with any evidence of COPD. Even in mild disease, cough may be troublesome and interfere with voice communication. Cough syncope may cause sudden incapacity. Impaired ventilation of parts of the lungs, or ventilation-perfusion mismatch, may be compatible with normoxaemia at ground level. However, the aircrewman with COPD is liable to be nearer the steep part of the oxygen dissociation curve, and ambient cabin altitudes even of civil aircraft (6K feet) and much more, of some military types (e.g., 17K feet) may induce definite desaturation. The effects of emergency decompression will be correspondingly more marked in smokers than in non-smokers. A heavy cigarette smoker may in any case have lost up to 10% of his available haemoglobin as carboxyhaemoglobin. He will be more liable than a non-smoker to unpredictable non-effectiveness due to respiratory tract infections, and more liable to fly whilst requiring medication. The cigarette smoking aircrewman will in addition be increasingly liable to many non-respiratory diseases, many of which, such as coronary disease, are inapparent yet major threats to flying safety. Heavy smokers have a greater expectation of accident and injury.

The conditions of military flying will impose other stresses which the aircrewman with COPD is less able to sustain without penalty. For example, high +Gz forces tend to cause acceleration atelectasis, especially during inhalation of 100% O<sub>2</sub>, even in health. Such atelectasis must confer a greater physiological handicap in the presence of COPD. The work of breathing is increased in COPD, and tolerance of pressure breathing will be reduced. The severe hypoxic stresses of emergency cabin decompression and of seat ejection must be adverse. Cockpit fumes or other irritants, e.g., traces of chemical warfare agents, will cause more problems in COPD than in health. Vibration causes oscillatory movement of inspired gases and hyperventilation, impairs the efficiency of pulmonary gas exchange, and adds to the work of breathing(11). Cockpit oxygen systems inevitably increase the ventilatory dead space. Flying clothing, especially counterpressure anti-G suits of the most modern type which include the trunk, increase the work of breathing and impair ventilatory efficiency(12). The physical stresses of survival conditions, escape and evasion, are less tolerable, and an airman may be deprived of regular medication. In many ways the military aviator with COPD may be the "weak link" in

the chain where a "team effort" is essential for survival or mission accomplishment. Even in "straight and level" peacetime flying in transport aircraft, some of the stresses described by be experienced, as indeed they may be in civil aviation. In general, COPD is incompatible with the flying environment; licensing of even the mildest cases requires very careful consideration.

Detection of COPD at the very earliest possible stage, when intervention may be effective and a flying career salvages, is clearly desirable. As noted earlier, clinical examination at this stage is rarely helpful. Cigarette or cigarillo smokers should automatically be suspected of having early disease; Berend et al (13) report that up to one third of apparently "healthy smokers will have respiratory functional abnormalities on adequate testing. Spirometry, the commonly available screening test, is unfortunately not effective in the detection of early COPD, being affected by extraneous factors and individual motivation. Commander Gary Gray, our Director, has discussed the problem of early detection of small airways disease in our earlier Short Course Report (14) and his description of the test available in a respiratory laboratory will not be repeated in full. Two tests are particularly helpful. The single breath nitrogen test (SBNT) estimates the closure of small airways. Following maximum exhalation, (to Residual Volume, RV) the subject inhales a single breath of 100% oxygen to total lung capacity, TLC. As he exhales this breath, the nitrogen concentration of the expired gas is monitored continuously. At first, as dead space gases are analyzed, nitrogen concentration is low, but rises rapidly to a more or less horizontal plateau as the more peripheral airways are evacuated. Late in expiration, the small airways in the lower part of the lung close, and the final exhaled gases come from the apices of the lungs. As these upper parts of the lungs are less well ventilated, the final part of the exhaled gas contains relatively less of the inhaled oxygen and nitrogen, so there is a sharp terminal upstroke in the more nitrogen concentration at the end of forced expiration. The volume under this terminal upstroke is called the "closing volume", i.e. the volume exhaled after closure of the small airways in the lower parts of the lungs. Closing volume is increased in smokers and in those with small airways disease (early COPD).

A refined test of airways resistance is the "Heliox" Test in which the subject performs spirometry while breathing a mixture of 80% helium, an inert, biologically inactive gas, and 20% oxygen. This gas mixture is much less dense than air, and normal subjects show a correspondingly increased expiratory flow rate when breathing heliox. In health, most of the resistance to air flow comes from the large central airways where flow is turbulent, and therefore much affected by gas density. Flow in the small distal airways is laminar and therefore not much affected by gas density. Where there is an increase in airways resistance, a central cause (e.g., tracheal compression) will tend to show an improved

performance with heliox; by contrast, predominantly small airways disease will cause airflow resistance that shows little improvement with heliox.

The diagnostic usefulness of respiratory function tests has been assessed by several authors. Cosio et al (15) found that both the heliox and SBNT tests were most sensitive in the detecting of early small airways disease, as judged by histological criteria. Spirometry was less sensitive. Berend et al (13,16) however found spirometric data to correlate best with overall histopathological abnormality, though the SBNT was more sensitive in detecting inflammation. Petty et al (17) also found good correlation between histological changes and the SBNT and heliox test results in mild or moderate emphysema. Dosmand and Cotton's (18) work however showed that the SBNT was at best 65% sensitive and that "false positives" were quite common. One must conclude that none of these tests is infallible but that a combination of spirometry flow-volume curves, SBNT and heliox tests, especially when serial results over several years are available, gives an excellent chance of detection of early COPD.

The aircrewman with early COPD should be restricted from high performance flying and receive clear, unambiguous advice on lifestyle modification, notably on quitting smoking. The airman who follows this advice, especially if he adopts other measures such as a regular aerobic exercise program, alcohol and weight restriction, may show remarkable improvement (19) and recover to meet the standards for unrestricted flying duties. However, nicotine addiction ensures that the craving for tobacco may take years to disappear; return to smoking is commonplace. Even the most determined ex-smoker may require an extended period of restricted flying, e.g., as or with co-pilot, on tanker-bomber-transport aircraft. Some may complete their careers in this role. Those showing deterioration, many of whom will be persistent smokers, must be permanently grounded. Fortunately this outcome is rare.

This section has indicated the overwhelming importance of tobacco smoking, especially cigarette smoking, in the aetiology of COPD. Smoking predisposes to other chest diseases such as cancer, acute bronchitis and tuberculosis. Numerically even more important is its place in the causation of cardiovascular disease, notably coronary and peripheral arterial disease. When one considers the large number of other disorders either caused or aggravated by smoking, nearly all of which can be prevented or improved by avoidance of the habit, it is clear that tobacco smoking is overwhelmingly the most important single health risk in the developed world (and increasingly elsewhere). The flight surgeon who successfully persuades his aircrew to give up smoking for life has made a major contribution both to their well being and to flying safety.

Strategies for achieving this goal may be considered under the following headings.

1. Personal advice. In the UK, studies show that brief (5-minute) interviews with patients by their general practitioners, consisting of little more than firm, uncompromising advice to quit, persuade about 5% to stop smoking. Many of these patients are symptomatic, and may have fears, justified or otherwise, of smoking-related diseases. They may therefore be more strongly motivated than a healthy aviator to follow advice. On the other hand, aircrew are more intelligent and better educated than the majority of patients, and have a strong vested interest in health maintenance and flying safety. Also, flight surgeons have time and opportunity for discussion of personal health habits during aircrew flight physicals as well as clinical consultations. For these reasons, opportunistic counseling of aircrew on their smoking habit is well worth-while. Studies suggest that verbal advice is more likely to be heeded if backed by printed and illustrated "hand-outs" - concise, often entertaining booklets that can be read in a few minutes.

2. Group therapy. Smoking cessation clinics may be helpful. They are conducted by a nurse or other health educator with a special interest in the topic and a large experience of the difficulties smokers encounter when trying to "kick the habit". The health professional will have more time than the flight surgeon to explain, illustrate and persuade; educational aids are available, smokers will attend repeatedly, will know that their achievements or failures will be exposed to peer scrutiny, and should benefit from mutual support, encouragement and success. Promotion of other health measures, e.g., daily aerobic exercise, is likely to be incorporated in the group therapy; regular exercisers are much less likely to smoke.

3. Drug treatment. This can only help those who are already motivated to quit, but who have strong physical and psychological dependent on the smoking habit. About 50% of all smokers have no such dependency; in most others, however, there is addiction to nicotine which, in the estimation of the United States Surgeon-General, may be as powerful as addiction to narcotic drugs. Nicotine chewing-gum, nicotine skin patch treatment or snuff will raise blood (and presumably central nervous system) nicotine levels sufficiently to suppress the craving to smoke, in most subjects (although many commercial (6)-available patches fail completely to produce such levels). The user should be committed to a program of progressive reduction in regular nicotine doses over a period of 6-12 weeks though occasional "ad hoc" use during subsequent difficult times may be helpful. Rather often, unfortunately, users of these smoking substitutes are both strongly addicted to nicotine and ambivalent towards quitting; a rather unsatisfactory long-term result, reduced smoking supplemented by use of gum or patches, may have to be accepted.

Hypnosis, acupuncture and other measures are often tried but appear to have a low long-term success rate.

4. **Social factors.** The attitudes and examples of family, friends, professional advisers and society generally are very important. The aviator who enjoys a stable marriage but whose wife is eloquently opposed to his smoking habit, whose teenage children regard it as "square", old-fashioned or disgusting and who banish him to the out house if he insists on smoking at home; whose colleagues are mostly non-smokers, intolerant of tobacco-smoke in the crew-room and mess; and whose flight surgeon is enthusiastic, supportive and a non-smoker, has a better chance of quitting than an individual without such backing.

5. **Political and fiscal factors.** High and rising taxes on tobacco, raising the cost progressively over other increases in the cost of living, deter some smokers, as do loaded insurance premiums. Enforcement of laws against sales to under-age smokers, with significant penalties for offending retailers; and advertising restrictions, notably on sports sponsorship by tobacco companies, are effective. Governments may agree to finance campaigns using media and advertising for anti-smoking publicity. Smoking bans in public areas, theaters, cinemas, restaurants, etc., are now common; provision of designated smoking areas, preferably remote, inconvenient and uncomfortable, is required.

The cumulative effect of all these measures will eventually persuade all but the most intractable smoker that the habit is more trouble than it is worth. Indeed, large studies have shown that at least half of all smokers do not enjoy smoking, and many are receptive to any reasonable suggestion to help them stop. Majority public opinion is now opposed to smoking; the time is right to convince the flying community that the aviation world is a smokeless zone.

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## SARCOIDOSIS AND THE AVIATOR

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Sarcoidosis is a chronic granulomatous disease of unknown aetiology. It is of particular importance in clinical aviation practice, for a number of reasons (1). Although it is a world-wide disease, it appears to be much more prevalent in the populations of developed countries. It is common in young adults; in Europe, more men than women being affected, but possibly the reverse in the USA (2). The onset may be acute and incapacitating, for example with florid erythema nodosum and acute arthropathy. Other cases are asymptomatic and may be detected only by special tests, e.g., screening chest x-ray (3), ECG or blood biochemistry. Though often apparently confined to the thorax, sarcoidosis is typically a multi-system disease with involvement, often silent, of many organs; the skin, eyes, liver, spleen, lymph-nodes, bone, central nervous and cardiovascular systems all being commonly affected. Hypercalcaemia is quite a common feature but causes symptoms only when potentially dangerous blood calcium levels are attained. No curative treatment is known, but moderate, severe or progressive disease usually leads to steroid treatment which may have to be prolonged and given in high doses. Cardiac involvement is often inapparent (4,5) but can be present with incapacitating arrhythmias, complete heart block

with Stokes-Adams attacks, or sudden death. The table summarizes the aspects of main aeromedical concern. Clearly, a disease of this type is a major potential threat to flying safety.

The frequency of cardiac involvement is uncertain. Dr H.A. Fleming (6), a British cardiologist, has made a life-time study of (at the most recent count) 300 cases which include 138 fatalities. Rhythm disorders, ventricular or supraventricular, were much the commonest clinical presentation. Various types of heart block occurred in 61% of cases, 26% showing complete (3rd degree) heart block. A "cardiomyopathic" picture was seen in one quarter of cases and apparent myocardial infarction in 5%.

Undoubtedly this series is weighted towards severe and fatal disease, as many cases were included from autopsy reports. However, cardiac involvement is well recognized, being present in 13-30% of those dying of sarcoidosis (3,4,7). In those patients diagnosed as having sarcoid heart disease during life, and coming to post-mortem, sudden death has occurred in up to 65% and congestive heart failure has occurred in a further quarter (3,8). Sudden death may be the presenting feature of sarcoid heart disease (9). There is agreement that the

### TABLE

#### FEATURES OF SARCOIDOSIS OF AEROMEDICAL IMPORTANCE

ONSET - Inapparent or Incapacitating

COURSE - Systemic upset  
 - Apparent cure  
 - Relapse - insidious, abrupt, late  
 - Chronic progression

MEDICAL CARE - Complex investigation  
 - Specialist follow-up  
 - Steroids

CARDIAC - Silent involvement  
 - Arrhythmias  
 - Heart blocks  
 - Heart failure  
 - Delayed manifestations  
 - Late deaths

NEUROLOGICAL - Brain, cord, peripheral nerves  
 - SOLs. Seizures. Meningitis

OPHTHALMIC - Recurrent inflammation. Visual loss.

METABOLIC - Hypercalcaemia, renal damage.



commonest clinical presentation is with arrhythmias and heart blocks (10). Heart failure, generally due to extensive myocardial sarcoid granulomas, quite often results from an unusual form of dilated cardiomyopathy, with akinesia, thinning or even aneurysmal dilatation of the upper inter-ventricular septum and left ventricular free wall and apparent normality of the cardiac apex (11).

(Sarcoidosis is one of the few types of heart disease, apart from ischaemia, causing focal wall movement abnormalities (12). Chest pain (anginal or "atypical") may be quite common (13), with abnormal thallium scans even in the presence of normal coronary angiograms. Microvascular spasm has been blamed, but a granulomatous sarcoid vasculitis also occurs.

Sarcoidosis in aircrewmen most often presents as bilateral hilar gland enlargement on a chest x-ray, often a screening film at a routine periodic flight physical examination but sometimes requested because of non-specific malaise or minor "bronchitic" chest symptoms - cough, scanty mucoid sputum or wheezing. Fine reticulo-nodular lung mottling, typically of the upper zones, is often associated. Similar x-ray findings occur in the other common clinical presentation; that is with erythema nodosum, often with acute arthropathy, confined to or most marked in the lower limbs. In this type, systemic upset with fever and high erythrocyte sedimentation rate is common, as is a raised concentration of angiotensin converting enzyme. A tissue diagnosis is established by bronchial biopsy or a positive Kveim test. Usually, other investigations are negative; bed rest and non-specific symptomatic treatment usually result in rapid clinical recovery, though the chest x-ray abnormalities may not resolve completely for 6 or 9 months or even more.

There is general agreement that this type of sarcoidosis has a prognosis far more favourable than when the disease presents in other systems (14,15,16). However, because of the risk of multisystem, notably cardiac or CNS disease, any aircrewman suspected of sarcoidosis should be immediately grounded and referred for full investigation (17). Cardiac investigation should await the resolution of acute symptoms. Tests will include serial 12-lead ECGs, a maximal exercise test, one or more 24 hour ECG (Holter) monitoring tapes, echocardiography and isotope studies, thallium and gallium scans. The multiplicity of tests unfortunately makes it likely that non-specific anomalies will be found, e.g., ectopic beats or an intraventricular conduction delay. A right-heart endomyocardial biopsy may be felt necessary to resolve such difficulties; but this is, because of the patchy nature of the disease a rather insensitive test (18).

Return to flying duties depends on the complete resolution of all evidence of sarcoidosis and the absence of any evidence of cardiac involvement. The earliest that flying fitness should be considered is one year after the initial diagnosis. In the RAF, pilots are usually awarded a restricted category at this stage,

A3, as or with co-pilot, sometimes also restricted from the stresses of high performance flight.

Specialist review with a complete non-invasive work-up is repeated after a further year. A completely satisfactory assessment allows return to unrestricted flying duties. However, specialist review every (2) years should be continued for the remainder of the airman's flying career.

The need for steroid treatment makes return to unrestricted duties less likely. No flying can take place until a satisfactory specialist review (12) months after cessation of treatment.

Sarcoidosis of other systems, especially ocular or nervous system, makes the prognosis less good and return to unrestricted flying rather improbable. A diagnosis of cardiac sarcoidosis entails grounding for life (16).

Applicants for military or professional civil flying duties who give a history of sarcoidosis should be refused (15). This decision rests on the possibility of inapparent and possibly undiagnosable persistent sarcoidosis which may produce abnormalities or incapacity during or after flying training.

The RAF experience of operating this policy over the past 14 years has been favourable. Of 24 aircrewmen diagnosed, 22 have been returned to flying duties, ultimately with no restrictions in any case, other than the need for indefinite specialist follow-up. One navigator was grounded permanently for cardiac sarcoidosis, and a pilot for progressive pulmonary involvement and hypercalcaemia relapsing after an initial course of steroids. It is believed that the United States Air Force experience is almost as favourable (2).

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## SPONTANEOUS PNEUMOTHORAX, CYSTS AND BULLAE

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Spontaneous pneumothorax is defined as the presence of air in the pleural cavity without apparent cause (1). Pulmonary conditions such as tuberculosis or cancer may cause spontaneous pneumothorax, but are excessively rare in aeromedical practice. The usual victims are apparently healthy young men, often in the third decade of life, very often tall and of lean, asthenic build. The chest x-ray may be normal before or after the illness, but may show sub-pleural blebs or small cysts, usually at the lung apex; the rupture of a bleb creates a broncho-pleural communication and the natural elastic lung recoil plus negative pleural pressure draws air into the pleural space. Consequent pulmonary collapse and contraction will narrow and perhaps seal the defect, which usually closes spontaneously in a few days. However the air may take several weeks to re absorb fully, especially if the pneumothorax is large, so that some form of evacuation of the air, e.g., by underwater seal or flutter valve, is usually desirable for any but the smallest pneumothoraces. The disease is disproportionately important in aeromedical practice, for various reasons.

The overall incidence of spontaneous pneumothorax is about 4.7 per 100,000 per year, but will be much higher in the young predominantly male world of professional aviation. It may cause sudden and unpredictable incapacitation. The pleuritic type of pain associated with pneumothorax is quite often severe and in any case must be distracting. A moderate sized pneumothorax may cause little functional disturbance at ground level, but will expand according to Boyle's law with the lower pressure at altitude, where it will cause increasing respiratory embarrassment and hypoxaemia due to ventilation/perfusion mis-match in the partially collapsed lung. A tension pneumothorax results from a flap-valve or one-way character of the pleural breach; the pneumothorax expands to fill one hemithorax then displaces the mediastinum to compress the other lung; this is an acute medical emergency and may be fatal. Many pneumothoraces cause a small pleural effusion, but sometimes this may be substantial. Haemorrhage (rare) causes a haemothorax; the blood does not clot, and the patient may collapse from exsanguination. In about 10% of patients, the disease will recur in the contralateral hemithorax; in 2.5%, the bilateral pneumothoraces are simultaneous, a very dangerous situation. There is a real risk that the physical conditions of flying, especially of flying high-performance military aircraft, may precipitate a pneumothorax; apart from rapidly varying cabin altitudes, stresses such as high G forces, vibration, sudden decompression, pressure breathing and emergency ejection might be expected to traumatise

the pleura. Actual records of spontaneous pneumothorax occurring in flight are however rather rare (2,3,4); occurrence during rapid decompression in an altitude chamber may be commoner (5).

Individuals who have recovered from spontaneous pneumothorax are prone to recurrence. After the first attack, the risk is 30%, after 2 attacks 50% and after 3 attacks 80%. Although most attacks recur within 2 years of the earlier episode, the timing of a recurrence is completely unpredictable.

This degree of risk precludes the return of a medically-treated aviator to flying duties, at least for a period of some years, and then only with a safety or co-pilot. For this reason aircrew are advised to undergo surgical treatment which consists of thoracotomy, identification and over-sewing of any pleural blebs or other abnormalities, and as complete a stripping of the parietal pleura as is possible (6). This apparently radical surgery is tolerated surprisingly well; patients are usually mobile from the first or second post-operative day, can be discharged from hospital in 7 to 10 days, and returned to unrestricted flying duties after review at 3 months. "Tests of cure" involving attempts to induce an artificial pneumothorax are no longer considered necessary.

Unfortunately this approach fails to deal with the small but real risk of contra-lateral recurrence. Identifying individuals at risk is difficult; but there is now evidence that nearly all patients with spontaneous pneumothorax have congenital bronchial abnormalities which are usually bilateral (1). The increasing availability of scanners (computerized tomographic or magnetic resonance imaging) should make it possible to detect contralateral lesions which may not be visible on conventional radiographs. However this is not routine practice in the RAF; it is felt that most such contralateral blebs would be small (less than one cm) and it would be difficult to justify bilateral surgical intervention, even if the patient would be prepared to submit to a double procedure (3). In practice, a contralateral pneumothorax in a patient with a normal chest x-ray has proved extremely rare. Unilateral pleurectomy remains the standard treatment. The less effective treatment of pleurodesis by closed pleural instillation or irritant fluids (7) has been obsolete for some years, though there are still advocates of pleurodesis (or partial pleurectomy) carried out during thoracoscopy, when superficial blebs can also be identified and oversewn (10).

Applicants for flying training who give a history of spontaneous pneumothorax will very rarely have been treated surgically, though a few will seek surgery should they believe this offers a change of acceptance. In the past, the RAF has accepted applicants with a remote history of a single attack, sometimes after as short a period as 2 years. This was justified by the relatively low lifetime risk of recurrence at this stage, probably 5-10%. However, in a contracting air force requiring fewer recruits, it is now felt that even this small risk of incapacity if unacceptable; at least for the time being, a history of spontaneous pneumothorax at any age is disqualifying for recruitment to flying training. The position of surgically treated applicants has not been defined but it seems likely they also will be excluded. Medical opinion however is that the risk remains fairly remote, and individual exceptions to the policy may well be made for non-pilot aircrew, e.g., cabin crew in multi-engine aircraft. For civil flying, private or commercial, a candidate with a remote history of spontaneous pneumothorax and a current normal chest x-ray is probably acceptable and eligible for an unrestricted license. However commercial airlines might well reject such an applicant for career flying.

#### CYSTS AND BULLAE

The distinction between cysts and bullae is not precise. A bulla is defined as an emphysematous space greater than 1 cm in diameter (8). This definition implies that bullae are related to the emphysematous process, i.e., generalized lung parenchymal disease; this is very often true, but localized lesions consisting of one or more bullae may sometimes be seen where the rest of the lung is normal. Cysts are other types of hollow lesions in the lungs and have many causes, ranging from congenital defects to cavitating (necrosing) tumours or inflammatory masses; they may also be single or multiple.

A bulla or a cyst may be closed or may communicate with an airway. A closed cyst is potentially more dangerous than a communicating cyst because it will expand as the ambient pressure falls (at altitude). The wall may rupture causing haemorrhage, surgical (mediastinal) emphysema, pneumothorax or even air embolism, with resulting pain, incapacitation or collapse. A communicating cyst should equilibrate with the ambient pressure and be less dangerous; though the effects of sudden loss of cabin pressure, ejection or pressure breathing could be adverse.

Many patients with a bulla or cyst, and most with more than one lesion, will have generalized emphysema or other lung disease and will be unfit to return to flying duties. Where there is a single lesion and overall respiratory function is normal or nearly so, consideration should be given to surgical excision. The larger the cyst, the stronger the indication; a few cysts and bullae enlarge progressively, possibly due to a partial one-way communication with an airway, and may eventually simulate the clinical and even radiological features of a tension pneumothorax. A

few patients with medium-sized or large cysts may have considerably impaired respiratory function, suggesting generalized lung disease, e.g., COPD, but recover completely normal function after the cyst has been excised. Where the bulla or cyst is small and unchanging and no serious underlying pathology is suspected, the patient may not wish to undergo surgery; a chamber ride to the maximum anticipated cabin altitude, if possible with a chest film at altitude to exclude enlargement of the radiolucent areas, may help in determining a return to some forms of flying, with suitable restrictions.

Apart from attempting to establish the aetiology of a cyst, pre-operative assessment concentrates on efforts to exclude inapparent disease elsewhere in the lungs. Computerized tomography, magnetic resonance imaging and isotope ventilation and perfusion scans are more sensitive than traditional contrast bronchograms and tomography.

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## ASTHMA IN AIRCREW

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### DEFINITION AND PATHOGENESIS

Asthma is a disease characterized by airway inflammation and increased bronchial reactivity. Symptoms, which characteristically are variable, include wheezing, shortness of breath, chest tightness and cough with sputum. In the past, attention was focused on the airway hyper-reactivity with bronchospasm and wheezing and treatment was directed towards bronchodilation as first line therapy. In recent years the central role of airway inflammation in the pathogenesis of asthma has gained increasing recognition (1). Airway inflammation is present in even mild asthmatics (2) and treatment of asthma has evolved towards more aggressive management of the underlying inflammatory response as a key element in control (3).

There are a number of triggers of the asthmatic response (inflammation/bronchospasm):

TABLE 1

TRIGGERS OF ASTHMA
<ul style="list-style-type: none"> <li>• Allergens</li> <li>• Occupational sensitizers</li> <li>• Respiratory infections</li> <li>• Additives - food, beverages</li> <li>• Drugs - <math>\beta</math> blockers, NSAIDs</li> <li>• Cigarette smoke</li> <li>• GE reflux</li> <li>• Exercise</li> <li>• Cold air</li> <li>• Air pollution</li> <li>• Emotional stress</li> </ul>

Asthmatic individuals exposed to inhaled allergens frequently show a dual airway response with an immediate airway bronchoconstrictor response beginning within a few minutes of exposure, followed after 4-6 hours by a delayed or late asthmatic response (LAR). The late asthmatic response is characterized by increased airway responsiveness and bronchial inflammation, and is less responsive to bronchodilator therapy. Mast cell degranulation is recognized as an important mechanism in the immediate response, and in modulation of the LAR (8). The eosinophil is increasingly implicated as being pivotal in the inflammatory reaction of the delayed response. (5)

The recognition of the late asthmatic response and of the chronic inflammatory nature of asthma has important implications in aircrew in that antigen exposure hours before flight can become manifest as severe bronchospasm during flight. On the positive side, control of inflammation with inhaled anti-

inflammatory medications may markedly reduce the requirement for  $\beta$ -agonists which are generally considered incompatible with flying duties.

### EPIDEMIOLOGY/NATURAL HISTORY

The prevalence of asthma in the general population is about 5% (4). The incidence and severity of asthma are rising in most countries with morbidity and mortality on the increase despite increasing use of anti-asthmatic medications. In fact, there is growing evidence that the cause may be related to increased use of beta-agonists (7). A possible explanation is the adverse effect of beta-agonists on the anti-inflammatory properties of the mast cell (8).

There is a clinical dogma that children with mild asthmatic symptoms will "grow out of it" during adolescence, and natural history studies do indicate that asthma which manifests in childhood may remit in adolescence, but this is far from being universal. Two longitudinal studies, one in Australia (6) and the other in the United States (4) demonstrated that even in those children with the mildest asthmatic symptoms, 45% went on to have further episodes of wheezing. The probability of recurrence in children with more frequent symptoms (more than 5 episodes in childhood) was even higher. This information is important in selecting candidates for aircrew training who have a past history of wheezing in childhood. Many airforces reject candidates with any history of wheezing in childhood; this conservative approach is certainly the safest, but in some countries (such as Canada), human rights issues preclude such a blanket approach and a more selective approach is required.

Individuals with asthma present a wide spectrum of severity from mild symptoms requiring intermittent inhaled bronchodilators only on challenge with heavy antigen loads or with respiratory infections through to patients with chronic severe symptoms who require daily inhaled and systemic medications. Indeed, there is a normal distribution of bronchial reactivity in populations, and not all individuals with bronchial hyper-responsiveness have clinical manifestations of asthma (9). One of the challenges facing those practicing aviation medicine is to identify and screen out asthmatics applying for aircrew training and to quantify the severity in trained aircrew presenting with asthmatic symptoms to facilitate a rationale aeromedical disposition.

## AEROMEDICAL CONCERNS IN ASTHMA

The aeromedical concerns regarding asthma include the possibility of acute incapacitation due to severe bronchospasm, performance degradation due to lesser degrees of wheeziness nonetheless disconcerting, side-effects of medications, the possibility of lung rupture in the event of rapid cabin depressurization with trapped gas which may occur in asthma, aggravation of mild hypoxia due to ventilation-perfusion mismatching, and increased risk of acceleration atelectasis in fast jet aircrew.

TABLE 2

AEROMEDICAL CONCERNS OF ASTHMA
<ul style="list-style-type: none"> <li>• Acute incapacitation</li> <li>• Performance degradation</li> <li>• mild bronchospasm</li> <li>• hypoxia</li> <li>• Side-effects of medications</li> <li>• Lung rupture with rapid cabin depressurization</li> <li>• Acceleration atelectasis in fast jet aircrew</li> <li>• Ability to wear protective equipment for extended periods.</li> </ul>

## SCREENING AIRCREW CANDIDATES FOR ASTHMA

Because of the high cost of training of military aircrew and the economic constraints now prevalent in all NATO countries, it is increasingly important to screen out asthmatic individuals applying for aircrew training. Because asthma is characteristically a disease with intervals free of symptoms and signs, the history is important yet may not be reliable in candidates. Candidates should be questioned by means of a signed and witnessed questionnaire about symptoms of wheeziness or recurrent respiratory problems in childhood (recurrent or chronic cough rather than wheezing may be the main manifestation of asthma in childhood); about other atopic and allergic symptoms including eczema, allergic rhinitis, food allergies; and about family history of atopy and asthma.

Physical examination is generally unhelpful in the detection of mild asthma; a decline in peak flow rate of at least 25% is required to produce an audible wheeze (10). However, signs of atopy should be sought including nasal examination for congestion, signs of atopic rhinitis or polyps, and observation of typical "atopic facies" with suborbital edema.

Assessment of candidates should also include objective assessment of airway function by pulmonary function testing. Routine spirometry may show mild expiratory airflow limitation but may well be normal in most mild asthmatics during symptom free intervals. An increase in flow rates of 20% or greater after bronchodilator inhalation is strongly suggestive of increased bronchomotor tone.

Candidates with any evidence of expiratory airflow limitation on routine spirometry or in whom there is any historical information to suggest asthma should undergo bronchial challenge testing with methacholine or histamine to assess airway reactivity, performed with a standardized methodology (13).

Such an approach has been found useful in detecting asthmatic candidates in the Canadian Forces (11) and by the Italian Air Force, who have further refined identification of atopic individuals with a multiple-allergen RAST assay (12). Methacholine sensitivity can be defined as the percent concentration which produces a 20% fall in FEV1 below baseline value, or PC20, or an index of cumulative dose, the PD20. In general, individuals who respond with a PC20  $\leq$  4 mg/ml have a strong probability of having asthma; this is used as the cut-off point for pilot selection in Canada (11). However, airway reactivity may vary with an individual's clinical status and normal airway reactivity at any particular time does not entirely preclude the possibility of past or future asthma (14). Recent undisclosed use of an inhaled bronchodilator or antihistamine may also produce a "false negative" test of bronchial reactivity.

## ASTHMA IN TRAINED AIRCREW

Although the majority of adult asthmatics will have "footprints" of previous asthma in the past, the initial presentation of asthmatic symptoms in adulthood is not a rare occurrence, and does occur in trained aircrew. Asthma accounted for almost half the groundings for respiratory problems in the survey presented in the Introduction to this AGARDOgraph. This most commonly occurs in conjunction with a respiratory tract infection frequently in association with exposure to a heavy allergen load or bronchial challenge such as vigorous exercise in cold air.

The diagnosis of "asthma" in trained aircrew is disconcerting to aeromedical authorities because of the concerns listed in Table 2 above and requires specialist referral for a careful evaluation including a detailed history, pulmonary function testing and bronchial challenge testing. The important task is to sort out where in the spectrum of bronchial hyper-reactivity and asthma the aircrew falls. This assessment must be based on the clinical evaluation, requirement for medication and on the results of bronchial challenge testing. Additional testing including bronchial reactivity to cold air and/or exercise, and testing for atopy by skin prick or multiple -antigen RAST may be helpful in the assessment. This will then aid in the determination of medication requirements if any, and the appropriate aeromedical disposition.

**Treatment:** Initial treatment should be aimed at removal of or avoidance of any inciting antigens such as pets, feather or down clothing or bedding, or others especially if positive on skin testing or RAST. Asthmatic aircrew who smoke must stop and are generally highly motivated to do so since their career may be in jeopardy; the implications must be clearly

explained and assistance and advice offered. The aircrew should know that smoking cessation has a positive effect on airway reactivity and may normalize mild airway hyper-reactivity and eliminate some requirements for medication.

Advice should be given to seek prompt attention for respiratory infections; in aircrew with mild asthma, the decision whether or not to treat with antibiotics may be made in favour earlier in the course of the illness.

In terms of medications, in general inhaled anti-inflammatory medications should be used aggressively to reduce the inflammatory component and to reduce the requirement for  $\beta$ -agonists. The side-effects of inhaled sodium cromoglycate and inhaled steroids are minimal and are not of aeromedical concern. Cromolyn can reduce the immediate and delayed LAR, while inhaled steroids are effective in reducing the late but not the early response. Both can be used to reduce the inflammatory component of asthma.

Inhaled  $\beta$ -agonists such as salbutamol, albuterol and terbutaline produce adrenergic systemic side-effects including tachycardia, anxiety, and tremor and are not compatible with flight duties particularly in flight deck aircrew. In addition to the undesirable side-effects, an acute requirement for bronchodilator medication is indicative of a degree of asthmatic instability incompatible with aircrew duties.

Systemic medications including theophylline, steroids or  $\beta$ -agonists are incompatible with flight duties and their use requires grounding of the aircrewman.

#### Aeromedical Disposition:

Aircrew who present with asthmatic symptoms such as wheezing must initially be grounded while investigations and appropriate treatment are initiated. At a minimum this should be 30 days but may be up to several months.

Flight deck aircrew and pilots of other than fast jet aircraft can safely be returned to flying duties with mild asthma well controlled with inhaled cromolyn and/or inhaled steroids alone. Normal pulmonary function and normal or near-normal bronchial reactivity ( $PC_{20} \geq 4$  mg/ml) should be confirmed after stabilization and while the individual is taking anti-inflammatory medication if required. Any additional requirement for  $\beta$ -agonists except in rare circumstances should be carefully reviewed and may require permanent grounding.

The presence of other than very mild reactive airways disease may require restriction from fast jets because of the chronic inflammatory involvement of small airways which may produce ventilation-perfusion mismatch in peripheral airways.

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## ARTERIAL HYPERTENSION AND THE AVIATOR

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Arterial hypertension is of great importance in the practice of clinical aviation medicine, mainly because of its prominence as a major risk factor for coronary artery disease and other disabling cardiovascular diseases, and because it is so common. Timely recognition of early or mild hypertension should facilitate appropriate intervention which will prevent complications and enable the aircrewman to continue his career, hopefully to normal retirement age. The consequent health benefits and fiscal advantages, both to the individual and to the air forces and airlines of the world, are obvious and substantial.

The World Health Organization (WHO) (1) has defined arterial hypertension as a systolic blood pressure (SBP) above 160 mm Hg and/or a diastolic blood pressure (DBP) above 95 mm Hg. Normotension is a blood pressure (BP) below 140/90 mm Hg whilst intermediate levels are "borderline". Labile hypertension means, literally, a BP sometimes above and sometimes below the upper limit of "normal"; but this applies to most mild or moderate hypertensives and in practice the terms labile, borderline and mild hypertension are used almost interchangeably. The WHO itself has recognized the impossibility of distinguishing normotension from mild hypertension; the choice of any level is arbitrary, at the frequency-distribution curve of human BP is curvilinear (a "log-normal" shape, or Gaussian curve with a "tail" to the right, or higher levels). Although the BP may be measured under carefully defined conditions (e.g., sitting, after 3 minutes' rest, right arm, relaxed conditions, controlled ambient temperature, standard time of day, fasting or otherwise, no prior vigorous exercise, etc., etc.) no protocol, however rigorous, can control the vast variation in arousal in an individual subject, based on personality of patient and examiner, perceived threat and anxiety, and many other factors. Furthermore the significance of a given BP level varies by up to 2 orders of magnitude depending on associated risk factors, evidence of complications, and the largely imponderable matter of individual vulnerability. These facts make generalizations on mild hypertension extremely difficult. However it remains true that any elevation of BP in an aviator should be taken seriously, and that the higher the level, in general the more serious the situation (2).

Arterial hypertension is extremely common. In the USA, up to 35 million people are said to have established hypertension and a further 25 million to have borderline hypertension (3), together constituting no less than 45% of the adult population!

Figures for the flying population are not readily available, though a much lower prevalence would be expected. However, hypertension was the main reason for referral of over 20% of all aircrew attending a specialist medical clinic in the RAF during 1991.

### Clinical Assessment

Assessment of an aviator with a high BP reading begins with an attempt to determine the "true" or even "basal" reading which may be more representative than a single casual reading. The problem of "white coat hypertension", where the elevated BP is partially or even completely attributable to an alerting or arousal reaction, is particularly acute in the aviation medical situation. The pilot is well aware that continuation of his flying career and livelihood depend on the finding of normotension. However he may also be aware that borderline or raised levels have been determined at previous examinations (56); he may have failed to implement the corrective measures advised at those times. He may find the examining medical officer's manner or personality to seem hostile, or more likely, he may perceive the whole procedure as threatening. These factors make it very unlikely that significant improvements will be found on repeated BP measurements during the medical consultation, or indeed on repeated consultations; Mancina et al (4), for example, found that the pressor effect of a doctor's visit to both normotensive and hypertensive patients was sustained to a considerable extent during his visit, and was virtually identical during a subsequent visit on another day. Rises of up to 75 mm in SBP and 35 mm in DBP were seen.

For these reasons, repeated BP measurements may be carried out by an automated static machine in the clinic, or by a clinic nurse (e.g., a 3-day check) or by the patient or a relative at home (5). Invariably the average of figures obtained in this way is lower than the figure(s) from the flight physical examination, but there are doubts as to the validity and accuracy of such records. The clinic nurse or spouse are seen as less threatening or even "on the patients side;" the accuracy of home machines is variable; preferred times of day may favour lower readings; personal habits (e.g., alcohol, exercise) may be temporarily altered to influence results; and frank falsification is possible. The phenomenon of "regression towards the mean" also operates.

Some of these objections are overcome by the use of ambulatory BP machines, ABPMS, which measure the BP non-invasively over a 24-hour period whilst the patient is ambulant and carrying out his normal duties. The technique has been in existence for



nearly 30 years but has recently gained rapid popularity with the introduction of small reasonably inexpensive self-powered machines with solid-state electronics and facilities for automated statistical analysis with digital and analogue summary and print-out. There are a few snags - measurements require the patients cooperation in limiting activity and will be inaccurate otherwise; but the accuracy and reproducibility of the method is now generally acknowledged (6). BP levels obtained by ABPMS are usually (7) but not invariably (8) lower than clinic levels, often much lower, such that 20-50% of patients previously diagnosed as having mild or moderate hypertension were found to be unequivocally normotensive in one review (9).

Advocates of the ABPMS point to its convenience and its reproducibility (6). The key question is whether the BP readings obtained by the ABPMS are more reliable than clinic BP levels in determining prognosis, in terms of event free survival. There is early evidence (10,11) that this is indeed the case, and that ABPMS results in addition correlate better than clinic BPs with the effects and benefits of treatment (12,13). It is however important to recall that the large population studies of the natural history of hypertension (14,15,16) and of the benefits of large-scale treatment (17,7) have been based on casual or clinic blood pressures; conclusive evidence of the superiority of ABPMS in this regard must await the results of large studies currently in progress.

Clinical assessment remains crucial in assessing level of cardiovascular risk, at whatever level of BP. Simple enquiry as to personal habits (exercise, smoking, alcohol, diet, medications) and family history (longevity, hypertension, heart disease, stroke, sudden death, diabetes, renal disease) is crucial. Aircrewmembers will almost always be, or claim to be, asymptomatic. Careful enquiry, especially concerning exertional symptoms ("indigestion", palpitations, pre-syncope) may however disclose potentially important symptoms which the aircrewman has discounted as physiological or trivial.

Physical examination is important, though usually normal. Obesity or lesser degrees of overweight are common and crucial in the aetiology of hypertension (18,3) but are easy to miss. Comparison of present body weight with weight at entry to flying training is often informative. Estimating the Body Mass Index (BMI), weight (kg) divided by height (m)<sup>2</sup> may help; BMI values below 24 lean, above 28 obese; but this will not distinguish overweight due to massive musculature and heavy build from obesity. Skinfold calipers give reproducible results and a reasonable estimate of the proportion of body fat (19). A subscapular measurement over 1.5 cm indicates excessive fat and over 2.5 cm, obesity. The sum of 4 skinfolds, subscapular, suprailiac, biceps and triceps, tends to give fewer abnormal results (less than 4 cm lean, over 8 cm obese). A relatively high subscapular value indicated predominantly central, male-pattern or upper truncal obesity which has more sinister prognostic significance (3).

Physical examination will otherwise concentrate on the cardiovascular system (pulses-tachycardia, irregularity, ectopics, delay, absence; cardiac impulse, murmurs, added sounds), the fundi, skin, chest and abdomen for signs of tobacco and alcohol use, and the fundi. (Hypertensive changes, even early, in the fundal arterioles indicate significant hypertension irrespective of BP levels obtained by the methods described). A check for proteinuria or glycosuria is essential.

#### Further Investigation

The further investigation of an aircrewman with suspected or actual hypertension will depend on available facilities. Complex investigations to exclude causes of secondary hypertension (e.g., pheochromocytoma, Conn's tumour or other adrenal gland disease, renal artery stenosis) are now rarely carried out in mild uncomplicated hypertension as the yield is too low and therefore the cost/benefit ratio too high. However some early cases of these diseases must be missed by this policy, which should be revised promptly when hypertension progresses, or resists standard medical treatments, or where there are unusual clinical or biochemical features.

A full blood count and a blood biochemical screen to include fasting blood lipids, preferably with HDL/LDL subfraction analysis, should be done; it will help in assessing overall risk and may disclose glucose intolerance or diabetes, renal impairment (rare) or alcohol and/or tobacco effects. Ultrasound examination of the adrenal glands and kidneys is well worthwhile and is adequate evidence of renal normality where the urine and renal function are normal. A chest x-ray may show cardiomegaly but changes, if any, are usually more subtle; prominence of the left ventricle, or unfolding or calcification of the aorta. (Embarrassingly, previously unsuspected aortic coarctation may be disclosed, usually in a recruit!).

The standard 12 lead scalar electrocardiogram, always required, may be within normal limits and yet show more or less subtle serial changes (increasing QRS amplitudes, lowering of T-waves) compared with earlier tracings; such alterations are important. Voltage criteria for left ventricular hypertrophy (LVH) are notoriously unreliable, being found, for example, in over 30% of healthy male RAF aviators (20); high QRS amplitudes are common especially in lean athletic young men. Conversely, hypertensive changes may be masked by obesity. Any evidence of LVH has major prognostic significance (21). Because of the insensitivity of the ECG in this respect, echocardiography should ideally be carried out in every case; echo is far more sensitive than the ECG in revealing LVH, found in 42% of established hypertensives (22) and 17% of borderline hypertensives (23), and has prognostic validity (24). Echocardiography may show evidence of diastolic

dysfunction such as reduced peak filling rate, but subtle changes in individual cases are hard to interpret as other common conditions (diabetes, coronary disease, obesity) may be the cause. Radionuclide (isotope) angiography is almost certainly more reliable in detecting early diastolic dysfunction (57).

Exercise testing may be carried out, usually to establish fitness level, exclude ischaemic heart disease or evaluate cardiac ectopic activity. Exercise has a poor discriminatory value in identifying borderline hypertensives (25), and hypertension is unfortunately a known cause of "false positive" ECG responses to exercise (26). A positive test may be repeated, probably with thallium scintigraphy, once the BP has been controlled; if again positive, the probability of coronary disease is high and coronary angiography will be required. Exercise testing may reveal LV functional abnormalities in hypertension even in the absence of coronary disease or early cardiac failure. Cuocola et al (58) found that about half of a group of hypertensives had diastolic dysfunction at rest (reduced peak filling rate and time to peak filling rate). These hypertensives showed an attenuated rise or even a reduced ejection fraction with exercise, which was also associated with a sub-normal increase in end-diastolic volume. Diastolic dysfunction was associated with a greater LV mass index in these patients; however diastolic dysfunction may precede definite LVH, and is probably one of the earliest markers of hypertensive target-organ damage and an indication for active anti-hypertensive measures.

#### Practical Management

Once these tests have been completed and reviewed, medical management decisions must be made. At the very least, indefinite follow-up with periodic specialist review will be required. In nearly every case, risk factors will have been identified that are amenable to correction or at least improvement. Stopping cigarette smoking in mild hypertension will confer greater benefits than any treatment of the blood pressure (17), and is the single most important measure in hypertensive smokers. Other physiological or non-drug measures have considerable attractions, mainly as they are essentially harmless or have minor, transient drawback, and also because they may confer very substantial benefits to other systems and to general health as well as lowering the blood pressure. Additional reasons for preferring physiological to drug treatments are the generally good prognosis of mild non-progressive hypertension when properly followed up; the knowledge that more than 40% of such cases may have a lower BP after several years' follow-up without treatment (27), whilst in the MRC trial (17) a similar proportion of placebo-treated patients were repeatedly normotensive after an average of 5 1/2 years; and uncertainty concerning the possible long-term effects of life-long drug treatment with medications often introduced only rather recently. An aircrewman judged suitable for

physiological treatment can usually continue his flying duties without restrictions.

#### Non-Drug Treatments

Non-drug treatments for hypertension have in the past decade been extensively investigated and reviewed (28, 29, 30, 31, 32, 33, 34). Controversy has centered on the efficacy of these measures, whether any effect is sustained, whether target-organ effects are arrested or reversed, and whether the proven benefits of drug treatment can be matched or even approached.

Weight reduction is the single most important measure, having been found effective by almost all investigators (34,35). Weight reduction is effective even where the patient is not apparently overweight (36). The mechanism is uncertain but is not merely an artifact due to reducing arm circumference. Suggestions include reduction in circulatory work, reduced alcohol; altered dietary constituents (notably sodium restriction), reduced catecholamine output and sympathetic drive to the heart, and increased physical activity. Weight loss short of the ideal is often effective. Schmieder (3) summarised 6 studies which found that weight reduction alone resulted in restoration of normal blood pressure in between 39 and 82% of patients so treated. Weight reduction was, in one study (37), found to be more effective than metoprolol in control of hypertension, whilst the same authors found that BP control by weight reduction has associated with reduction in left ventricular mass (38).

The main problem with weight reduction is patient compliance and persistence. Aircrew, who have so much to gain from the method, may be strongly motivated to cooperate, especially when counseled on ancillary benefits such as improved blood lipids, glucose tolerance, insulin resistance, etc. It is reassuring that BP control may survive some later regain of weight, which is however strongly to be discouraged at regular follow-up.

Weight loss and maintenance of a lean physique are greatly assisted by a graduated daily aerobic exercise programme. Regular exercisers are lighter and have lower blood pressure than sedentary individuals (39,40), and it is now accepted that this type of exercise lowers BP in hypertensive as well as normotensive people (32,41), may reduce LV mass (32) and plasma catechol amines in borderline hypertensives, and produces an effect within 10 days of commencement (42). The associated physical, biochemical and psychological benefits of regular physical exercise are so great that all hypertensive aircrewmen should maintain a lifelong exercise programme.

Alcohol is a pressor substance in more than moderate social amounts (2-3 u/d), and there is abundant clinical and epidemiological evidence (31,43,44,45) that alcohol plays an important part in sustaining raised BP in many hypertensives.

Stopping alcohol usually produces a rapid and sustained fall in BP (46,47) of variable but in some cases marked extent. Alcohol restriction will aid dieting, weight reduction, blood lipids, urate, etc., and should be encouraged in all hypertensives.

The other constituents of diet have a less certain effect on BP. Salt restriction has powerful epidemiological support (48) but a diet as low in sodium (70 mEq/d) as that seen in some isolated tribes, all of whose members enjoy life-long normotension, would be intolerable to most patients. Although a few patients, usually with fairly severe hypertension, respond very well to sodium restriction, overall results are mixed and unconvincing. Nevertheless some authorities (29,31,34) still advocated low-sodium diets, which are probably harmless and may be worth a trial in an aircrewman who is prepared to endure a relatively unpalatable diet. Potassium supplementation may have an additional hypotensive effect (33) but, as with calcium and magnesium supplementation, results are conflicting or unimpressive, and all these cations may have harmful effects in some people. The effects of a high-fibre, low saturated fat diet on the blood pressure are equally uncertain, but the overall benefits of such a diet would commend it for all hypertensives. Beilin (31) accepts that a vegetarian diet causes a fall in blood pressure which is unexplained. Cigarette smoking cannot be incriminated in the aetiology of hypertension, and in fact smokers tend to have lower BPs than non-smokers (49) and to experience a rise in BP when they quit (34), in part due to weight gain. However, so great are the health benefits of stopping smoking that the small pressor consequence must be accepted as a preferable penalty.

#### Drug Treatment

The decision to institute drug treatment for hypertension in an aircrewman is rarely easy. Treatment will almost certainly have to be life-long. The choice of drug and response to it will have effects, possibly profound, on the aircrewman's career, well-being and social existence. Although, happily, the first choice of drug may result in lasting good BP control with minimal or no side-effects, the decision to treat implies acceptance of a responsibility to secure good BP control, if necessary by repeated drug substitutions or additions (stepped care), a willingness to appraise subjective side-effects, short- and long-term, for acceptability or as an indication for change; preparedness to search for inapparent side effects during regular follow-up which must be life-long; and ability to reconcile the airman's clinical situation with the conditions and regulations of the flying environment.

The main indications for drug treatment are likely to be the overall level of cardiovascular risk both from hypertension and from other factors; apparently sustained or progressing BP level; failure or rejection of non-drug measures; or evidence of target-organ damage. Rose (50) has said that "the best clinical

definition of hypertension is the level of arterial pressure at which the benefits of intervention exceed those of inaction".

An aircrewman commencing antihypertensive drug treatment should be grounded until his BP is well controlled and side effects, if any, are confirmed as minimal and unimportant. A period of at least 4 weeks is needed but this may have to be extended where dose increases or addition or substitution of another drug (stepped care) are required. Where practicable, medical boards may return an aircrewman to temporarily restricted flying duties for an arbitrary period (e.g. 6 months) to limit risk and allow further observation. The choice of drugs should be limited to those authorized for use in aircrew.

Thiazide diuretics (51) were the first antihypertensive drugs tested specifically for their appropriateness in aviators. Over subsequent years, other diuretics, often combinations of a thiazide and a potassium-retaining diuretic such as amiloride or triamterene, have been used (Spironolactone is now obsolete). These drugs remain the first line of treatment in many air forces including the USAF and the RAF. Despite occasional side-effects such as impairment of glucose tolerance, hypokalaemia, hyperuricaemia and hyperlipidaemia, and clinical effects such as fatigue or impotence, the results of treatment remain generally good (52). There is no orthostatic effect and diuretics confer the unique benefit on a pilot that he may, if his BP is well controlled without side-effects or complications, be returned to full unrestricted flying duties with minimal subsequent inconvenience; compliance is good and the airman can be reassured that the benefits are more likely than not to be retained for the remainder of his flying career and beyond.

No other class of drug can match this success. Beta-blockers have been used in civil flying and in some airforces. A drug of low lipid and high water-solubility should minimize central nervous system involvement; cardio-selectivity should minimize toxicity, whilst a long-acting drug with a narrow dose range should assist compliance and reduce the period of grounding. In 1982 the RAF introduced atenolol for aircrew whose hypertension was uncontrolled by diuretics or in whom diuretics were contra indicated. The lowest possible dose was used (25-100 mgm/d) often in combination with a diuretic. Strict controls have been maintained (unfit single-seat operations or high-performance aircraft)/ Despite these constraints, and concern over experimental evidence of CNS effects (53), this treatment remains effective and has enabled several dozen aircrewmen to return to (restricted) flying duties.

In 1991, following research at the RAF Institute of Aviation medicine (54) and elsewhere, a decision was made to introduce the Angiotensin Converting Enzyme inhibitor enalapril for the very few aircrewmen whose hypertension could not be managed successfully by other acceptable drugs.

ACE inhibitors are known sometimes to cause an orthostatic fall in BP, and certainly affect G-tolerance (55), so the precautions used for atenolol also applied, with a number of added restrictions. So far 5 aircrewmen, none of them pilots, have been able to return to flying whilst taking enalapril, sometimes combined with a diuretic. These constraints may be unduly cautious. A case could be made out for allowing single-seat operations, even possibly fast jet flying, for an aircrewman with uncomplicated hypertension well controlled on an ACE inhibitor which caused no side-effects in that individual. The case would be based on the apparent superiority of ACE inhibitors (compared with other permissible drugs) in their absence of effects on cognitive function or body biochemistry, and of the fact that the orthostatic fall in BP is usually slight, comparable with the effects of physiological factors such as fatigue, thermal stress or dehydration. The aircrewman would have to demonstrate G-tolerance, protected and unprotected, within the normal range, and absence of side-effects notably cough and angio-oedema, which would be less likely after several months of trouble-free treatment.

Overall our present drug policy has seemed to work well. No instances of sudden incapacity in the air have been attributed either to drug treatment or to complications of hypertension. Side-effects appear infrequent. No aircrewman has been permanently grounded in the past 10 years solely as a result of uncomplicated hypertension. It seems possible that, in future, other drugs may be added to or substituted for the medications described. At present no recommendation for change is made, and indeed the need for other drugs in a rather small air force must be very limited. New drugs often have apparent, even major advantages, but the old should not be discarded until very clear evidence of advantage, preferable over a number of years is obtained.

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14. Abstract	<p>This Lecture Series will update the information presented in the 1987 AGARD Short Course on the Cardiopulmonary Aspects of Aerospace Medicine, and will be of primary relevance to military internists and cardiologists with an interest in aviation medicine, and to military Flight Surgeons. Topics to be discussed will include techniques for and utility of screening for asymptomatic coronary artery disease in an aircrew population; the aeromedical disposition of aviators with coronary disease; the usefulness of primary coronary prevention programmes, based on data from recent intervention studies and meta-analyses; the aeromedical implications of ECG abnormalities and structural/valvular cardiac anomalies based on data from USAF/AL Study Groups; the utility of screening aircrew candidates with echocardiography and echocardiographic findings in trained aircrew; hypertension in aircrew; and the aeromedical implications of a number of pulmonary diseases, notably asthma and airway hyper-reactivity, obstructive pulmonary disease, pneumothorax and sarcoid. The Lecture Series will be designed to be interactive rather than strictly didactic to encourage discussion of problems particular to participating NATO countries.</p> <p>This Lecture Series, sponsored by the Aerospace Medical Panel, has been implemented by the Consultant and Exchange Programme.</p>										



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